A STUDY ON
UTHIRA VATHA SURONITHAM
(Rheumatoid Arthritis)

Dissertation Submitted To

THE TAMIL NADU Dr. M.G.R. Medical University

Chennai – 32

For the Partial fulfillment for the Award of Degree of

DOCTOR OF MEDICINE (SIDDHA)

(Branch – III, SIRAPPU MARUTHUVAM)

DEPARTMENT OF SIRAPPU MARUTHUVAM

Government Siddha Medical College

Palayamkottai – 627 002.

OCTOBER - 2018

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BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled **"A STUDY ON UTHIRA VATHA SURONITHAM** is a bonafide work done by **DR. S. AYSHA, GOVERNMENT SIDDHA MEDICAL COLLEGE, PALAYAMKOTTAI** in partial fulfillment of the University rules and regulations for award of **M.D (SIDDHA), BRANCH - III SIRAPPU MARUTHUVAM** under my guidance and supervision during the academic year **2015-2018 OCTOBER.**

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"A STUDY ON UTHIRA VATHA SURONITHAM"** is a bonafide and genuine research work carried out by me under the guidance of **Prof. Dr. A. S. POONGODI KANTHIMATHI., M.D(s).,** HOD, PG - Department of Sirappu Maruthuvam, Govt. Siddha Medical College, Palayamkottai and the dissertation has formed the basis for the award of any Degree, Diploma, Fellowship or other similar title.

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Supervisor&Guide	Dr.A.S.Poongodi kanthimathi. M.D (s) Professor &Head of the Department
Dissertation topic	An open clinical Study to evaluate the clinical efficacy of siddha sasthric formulation "**MATHIYOOSHNA RASAYANAM**"(Internal) "**NYMPATHI THYLAM**"for the treatment of **UTHIRA VATHA SURONITHAM.**
Document field	1. Protocol2. Date Collection Form 3. Patient Information Sheet 4. Consent form5. SAE (Pharmacovigilance)
Clinical / Non Clinical trial Protocol	Clinical trial protocol – Yes
Informed consent document	Yes
Any other document	Case sheet, Investigation document
Date of IEC approval & it's Number	GSMC/3.IEC/2016/III-20/20.07.16

We approve the trial to be conducted in its presented form.

The Institutional Ethical committee expects to be informed about the process report to be submitted to the IEC at least annually of the study, any SAE occurring in the course of the study and changes in the protocol and submission of final report.

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20/7/2016
(Prof.Dr.M.Logamanian)

Member Secretary
20/7/16
(Prof. Dr.S.Victoria)

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This is to certify that the project **Evaluation of Anti-inflammatory, Analgesic And Toxicological Profile of Mathiyooshna Rasayanam** has been approved by the IAEC, KMCH College of Pharmacy, Coimbatore.

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17/12/18

Dr. D. Kannan
Main Nominee [CPCSEA]

18	Kandu parangi	Clerodendrum serratum	Verbinaceae	Root
19	Vetpalai	Wrightia tinctoria	apocyanaceae	Seed
20	Arathai	Alpinia galanga	Zingiberaceae	Rhizome
21	Vaaluluvai arisi	Celastrus paniculatus	Celastraceae	Seed
22	Korai kilangu	Cyperus rotundus	Cyperaceae	Root tuber
23	Nannari	Hemidesmus indicus	Asclepiadaceae	Root
24	Kostam	Saussurea lappa	Asteraceae	Rhizome
25	Sadaamaanjil	Nardostachys grandiflora	Valerinaceae	Root
26	Annachipoo	Illicium verum	magnoliaceae	Flower
27	Adhimathuram	Glycyrrhiza glabra	Fabaceae	Root
28	Kaattu milagu	Piper nigrum	piperaceae	Seed
29	Omam	Carum copticum	Umbelliferae	Seed
30	Mullai ver	Jasminum trichotomum	Oleaceae	Root

INGREDIENTS OF NYMPATHY THYLAM

S.NO	INGREDIENT	BOTANICAL NAME	FAMILY	PART USED
1.	Chadurakalli juice	Euphorpia antiquorum	Euphorbiaceae	Whole plant
2.	Maampattai chaaru	Mangifera indica	Anacardiaceae	Pattai
3.	Maangolunthu chaaru	Mangifera indica	Anacardiaceae	Leaf
4.	Maampoo chaaru	Mangifera indica	Anacardiaceae	Flower
5.	Erukkam ver pattai chaaru	Calotropis gigantea	Asclepiadaceae	Root
6.	Etti kottai	Strychnos nux-vomica	Loganiaceae	Seed

Station:

Date:

Authorized signature

Dr. S. SUTHA, M.Sc.,M.Ed.,Ph.D.,
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Certificate

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Conducted By

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This certificate is proudly presented to Dr. S. Aysha. P.G. Scholar

for the Participation in **"A Preamble of Pura Maruthuvam and its Clinical Application"**

held on 13-04-2018 at Government Siddha Medical College & Hospital, Palayamkottai.

13/4/18

Prof.**Dr. A.S. Poongodi Kanthimathi** M.D (Siddha).,
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This certificate is proudly presented to Dr. S. AYSHA P.G. Scholar

for the Participation and Implementation of **"International Day of Yoga"**

held on 21-06-2018 at Government Siddha Medical College & Hospital, Palayamkottai.

Yoga for Harmony & Peace

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SCREENING COMMITTEE

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This is to certify that the dissertation topic an open clinical study to evaluate the efficacy of siddha sashtric formulation "..MATHIYOOSHNA..RASAYANAM(INT)NYMPATHYJHYLAM(EXT) for the treatment of .....UTHIRA..VAATHA...SURONITHAM..... had been approved by the screening committee.

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II	Gunapadam	Dr.A.Kingsly MD(S) Associate Professor	
III	Sirappu maruthuvam	Prof.Dr.A.S.Poongodaikanthimathi MD(S)	
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CERTIFICATE OF BOTANICAL AUTHENTICITY

Certified the following plant drugs used in siddha formulation **MATHIYOOSHNA RASAYANAM (INTERNAL) & NYMPATHY THYLAM (EXTERNAL)** for management of **"UTHIRAVATHA SURONITHAM" (Rheumatoid Arthritis)** taken up for post-graduation dissertation studies by **Dr.S.AYSHA M.D (S)., (REG.NO:321513001)** PG scholar, department of sirappu maruthuvam are correctly identified and authenticated through Visual inspection / Organoleptic characters / Experience, Education & Training morphology, microscopical and taxonomical methods

INGREDIENTS OF MATHIYOOSHNA RASAYANAM

S.NO	INGREDIENT	BOTANICAL NAME	FAMILY	PART USED
1	Paranki pattai	Smilax china	Liliaceae	Root tube
2	Jathipathri	Myristica fragrans	Myristicaceae	Aril
3	Milagu	Piper nigrum	Piperaceae	Unriped fruit
4	Vaivilangam	Embelia ribes	Myrsinaceae	Dried fruits
5	Chukku	Zingiber officinale	Zingiberaceae	Dried rhizome
6	Santhanam	Santalum album	Santalaceae	Wood
7	Kadukkai	Terminalia chebula	Combretaceae	Pericarp
8	Thippili	Piper longum	Piperaceae	Fruit
9	Nelli paruppu	Phyllanthus emblica	Euphobiaceae	Dried fruit
10	Lavanga pattai	Cinnamomum verum	Lauraceae	Bark
11	Ealakkai	Elettaria cardamomum	Zingiberaceae	Seed
12	Kirambu	Syzygium aromaticum	myrtaceae	Flower buds
13	Thanri kaai	Terminalia bellirica	Combretaceae	Dried fruit
14	Sevviyam	Piper nigrum	Piperaceae	Root
15	Jeeragam	Cuminum cyminum	Apiaceae	Fruit
16	Thippili moolam	Piper longum	Piperaceae	Root
17	Krosani Omam Kandu parangi	Hyoscyamus niger Clerodendrum serratum	Solanaceae	Seed

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This Certificate is awarded to Dr/Mr/Mrs.....AYSHA.S.....

For participating as ~~Resource Person~~ / Delegate in the Twenty First Workshop on

"RESEARCH METHODOLOGY & BIOSTATISTICS"

*For **AYUSH Post Graduates & Researchers***

Organized by the Department of Siddha

The Tamil Nadu Dr. M.G.R. Medical University From 25th to 29th April 2016.

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ACKNOWLEDGEMENT

The author is extremely grateful to Lord Almighty who empowered the author with His blessings and grace to complete this dissertation work successfully.

I take this opportunity to express my gratitude to the Vice Chancellor, The Tamilnadu Dr.M.G.R. Medical University, Chennai and The Director. Directorate of Indian Medicine and Homeopathy, Chennai who flagged my dissertation with cheer.

My grateful thanks to **Prof. Dr. R. Neelavathy, M.D.(s), Ph.D.,** Principal, Government Siddha Medical College, Palayamkottai and **Prof. Dr. S .Victoria M.D (s)** Vice - Principal, Government Siddha Medical College, Palayamkottai for permitting me to make use of facilities available in this institution to bring out the dissertation, a successful one.

The author is grateful to **Dr.A.S.Poongodi Kanthimathi.,M.D(S).,** Professor, Department of Sirappu Maruthuvam, (P.G III),Government Siddha Medical College, Palayamkottai for her valuable guidance regarding these studies.

Would like to show my gratitude to Reader **Dr.M. Ahamed Mohaideen, M.D(s).,** Associate professor, Department of Sirappu Maruthuvam, (P.G III),Government Siddha Medical College, Palayamkottai for his kind guidance and good co-operation to make the easy way to complete the dissertation.

I would like to show my gratitude to Lecturer (Grade II) **Dr.S.Sujatha M.D(s).,** for her kind guidance and good co-operation to make the easy way to complete the dissertation.

I would like to show my gratitude to Lecturer (Grade II) **Dr.G.Ganesan M.D(s).,** for his kind guidance and good co-operation.

I would thank to Lecturer (Grade II) **Dr.R. Vanamamalai M.D (s)** for his kind guidance and good co-operation.

The author is thankful to **Mrs.Nagaprema M.Sc.,** Head of the Department Biochemistry, Government Siddha Medical College, Palayamkottai for all technical assistants of clinical laboratory for their help in evaluating the trial drugs.

The author is so grateful to **Dr. Mr. .Kalaivanan M.Sc.,M.Phil.,Ph.D** Lecturer, Department of Pharmacology, Government Siddha Medical College, Palayamkottai in carrying out the Pharmacological analysis of the trial drugs, needs special mention and appreciation.

I express my thanks to **Dr.S.Sudha, M.Sc., M.Ed., Ph.D.,** Associate Professor, Department of Medicinal Botany, Government Siddha Medical College, Palayamkottai for the guidelines in identification of herbal drugs.

I heartly thanks to my husband **Mr.M. Mohammed Riyaz** and My Father and Mother.

I sincerely thank the great **Siddhars** who show me the right pathway in Siddha system. My heartful thanks to my colleagues and friends for assisting and helping in many ways.

Finally, I am very thankful to the computer centre, **Mr. M.Maharaja**, for his kind co-operation in bringing out this dissertation work in an excellent format.

INTRODUCTION

Siddha system is a unique system of medicine because it is both spiritually and mentally enriched. Siddha system is one of the ancient system of Indian medicine. It evolved in south india and siddha medicine was developed by siddhars.

Our human body consist of 96 thathuvam,72000 nadi narampugal, 7 udal thathukkal, 3 uyir thathukkal and impalance in these constituents leads to rogum.

The normal functioning of human body is based on homeostasis of 3 forces or 3 humors called **VATHAM, PITHAM** and **KABAM.**

Any derangements in this homeostasis lead to pathological condition called **PINI** or **NOI**

Siddhars classified the diseases in to 4448 types. Among that vadha disease are classified in to 84 types mentioned in yugi vadhiya cinthamani.In which uthira vatha suronidham is one among them and signs and symptoms of this disease is correlated with Rheumatoid arthritis in morden science.

Siddhars diagnosing the diseases by means of envagai thervu, nadi, and neerkuri, neikuri are the Precise diagnostic stool of siddhars. The treatment aspect involve the neutralization of affected humour.

BY giving purgatives, vatha kutram is neutralized. By giving emetics, pitha kutram is neutralized. By giving nasiyam kapha kutram is neutralized

RHEUMATOID ARTHRITIS is an autoimmune disorder which is world wide in distribution. About 0.5 - 3% seems to be affected. Womens are affected 3 times more than men. It is present from early childhood (when it is rare) to late old age, most common in 30-50 y
It is the disease which causes much distress to the humanity at large. Till now there is no definite cure for this disease. Due to the prolonged and uncertain course of the disease and its prevalance the author planned to be conduct the study on **UTHIRAVATHA SURONITHAM**.

The author's choice of drug for clinical study were,

1. Mthiyoosna rasayanam- 6 gm twise a day internally
   [yugimuni Vaithiya Kaviyam. Page no: 283]
2. Nympathy thylam - externally [sarabenthirar vaithiya muraigal]

Siddha drug formulations has not undergone any clinical trial so

.AIM AND OBJECTIVES

AIM

The principal aim of the present study is to evaluate the therapeutic efficacy of the siddha formulations "Mathiyooshna Rasayanam" (Internal) and "Nympathy thylam" (External) in the treatment of "Uthiravatha suronitham" (Rheumatoid arthritis).

PRIMARY OBJECTIVE:

To Evaluate the Safety and Therapeutic efficacy of the siddha drugs "**Mathiyooshna Rasayanam**" (Internal) and "**Nympathy thylam**" (External) in reducing the pain in the treatment and restricted joint movements "**Uthiravatha Suronitham** (Rheumatoid Arthritis)."

SECONDARY OBJECTIVES:

- To conduct a clinical trail with a well defined proforma on identified patients with "UTHIRAVATHA SURONITHAM"**.**
- To correlate the etiology, clinical features, signs and symptoms of "UTHIRAVATHA SURONITHAM" in siddha system to Rheumatoid Arthritis in modern science.
- To study "UTHIRAVATHA SURONITHAM" on the basis of Mukkutram, poripulangal, udalkattugal, envagai thervugal in order to evaluate the pathology.
- To access the biochemical constituents of the drug.
- To perform the pharmacological analysis to evaluate the ANTI INFLAMMATORY, ACUTE TOXICITY AND ANALGESIC effect on internal medicine and ANTI INFLAMMATORY on external medicine.
- To conduct clinical study on "UTHIRAVATHA SURONITHAM" in both in patients and out patient department with reference to Age, Sex, Socio economic status, habits, family history etc on the disease.
- To access the effect of steam bath in Uthira vatha suronitham patients. To find out whether there are any side effects / adverse effects produced by the trial drugs Mathiyooshna Rasayanam (Internal) and Nympathy thylam (External) if any.
- To apply the modern parameters on investigation side and also NEIKURI on siddha aspect to confirm and follow the prognosis

SIDDHA ASPECT

PRINCIPLES OF SIDDHA

Siddhars have recommended certain basic guidelines to be followed for healthy living which includes following certain regimen as mentioned in" PINI ANUGA VIDHI" that help prevent disease. The rules are given below

1.Drinking boiled water

2.Take meals twise a day

3.Take diluted buttermilk and melted ghee

4.Take sufficient quantity of milk and milk products

5. Never eat root tubers except yam

6.Never consume food that was prepared the previous day

7.Always have food after feeling hungry

8.Always consume sour curd

9.Drink water at the end of meals

10.Practice walking after a good diet

11.Use hot water while taking oil bath

12. Take snuff medications eight times in a year

13. Take purgative medication every four months in a year

14. Take emetic medication once in six months

15.Never sleep during day time

16. Never suppress any natural urge

17.Always indulge in healthy sexual acts

18.Never sleep under a tree shade

19. Never smell fragrance during midnight

20. Never resides close to the dust

21.Apply eye medications once in three days

22.Shave weekly once

23. Take oil bath once in every 4 days

The siddha system is said to be the human body is composed of 5 elements such as :

EARTH- gives shape to the body and release site energy.Bones, muscle,and tissues if in the body

WATER-Makes earth supple and transmission of energy.Serum, lymph,saliva,etc., represent in the body.

3.FIRE- Makes the form of the body steady and gives vigour and stimulation. Digestion and circulation represent in the body.

4. AIR- Ignites the fire works as a life carrier and is the support of all contact and exchange respiration and Nervous system represent in the body

5. ETHER- It is the creator of life itself in the body.

A harmonious combination and function of these five elements in the body produce a healthy and beautiful life.

Characteristic features of Vatha diseases

1. Body ache
2. Nerve weakness
3. Dryness
4. Joint pain
5. Bony pricking pain
6. Constipation
7. Darkness of eyes,skin and urine
8. Mental distress
9. Difficulty to movement of limbs
10. Polydypsia

QUALITIES OF VATHAM

The normal qualities are

1.Rough

2.Dry

3.Light

4.Cold

5.Movable

6.Subtle

Opposite qualities of vatham

1.Soft

2. Untuous

3.Heavy

4.Hot

5.Stable

6.Solid

Relation with taste

CAUSES OF VATHA DISEASES

"பகரவே வாதமது கோபித் தப்போ

பண்பாக பெண்போக மதுதான் செய்யில்

நகரவே வெகுதூரவழி நடக்கில்

நளிரான காற்றுமே பனிமேற் பட்டால்

மிகரவே காய்கள் கனிகிழங்கு தன்னை

மிகவருந்தி மீறியே தயிர்தான் கொண்டால்

முகரவே முதுகெலும்பை முறுக்கி நொந்து

முழங்காலும் கனைக்காலும் கடுப்பு உண்டாமோ"

- *யூகி வைத்திய சிந்தாமணி பாடல் - 28*

Walking for long distance and harmful combinations like fruits, vegetables and tubers causes toxic factors which affects bones and joints.

According of Agathiar kanma kandam – 300

"நூலென்ற வாதம் வந்தவகை தானே

துண்மையாய்க் கன்மத்தின் வகையைக் கேளு

காலிலே தோன்றியது கடுப்ப தேது

கைகாலில் முடக்கியது வீக்கமேது

கோலிலே படுகின்ற விருட்ச மான

குழந்தை மரந்தன்னை வெட்டல்மேல் தோல் சீவல்

நாலிலே சீவசெந்து கால் முறித்தல்

நல்ல கொண்பு தழை முறித்தல்நலித்தல் தானே

- *அகஸ்தியர் கன்ம காண்டம் - 300 பாடல் 56*

Agathiar kanma kandam -300 attributes the following psychological factors such as, breaking the animal legs, removing the bark of living trees. Cutting the trees in the living branches and removing leaves to be the cause for vatha diseases.

UTHIRA VATHA SURONITHAM

Definition

Uthira Vatha Suronitham is a condition which deals with the involvement of joints which comprises the symptoms of pain and swelling mainly in the small joints and also in large joints with lassitude and anorexia

உதிரம், சுரோணிதம் - குருதி

வாதம் - வாயு + ஆகாயம்

இதனை வளி, சுற்று, காற்று, ஊதை, கால் என்றும் கூறுவர்.

வளி (வாதம்) தன் அளவில் மிகுந்திருக்கும் போது உடலில் வாதநோய்கள் தோன்றுகின்றன. "யூகி வைத்திய சிந்தாமணி" நூலின் படி

"என்னவே வாதமது எண்பதாகும்" என்று பாடினாலும் அவைகளின் பெயர்களையும், குணங்களையும் கூறும்போது எண்பத்தைந்து வகைகளைக் கூறியுள்ளார் அவற்றில் ஒன்று "உதிரவாத சுரோணிதம்".

Clinical features of uthira vatha suronitham

In Yugi Vaidhiya cinthamany

"வைகிதமாய்க் கணுக்காலு முழங்கால் தானும்

மற்கடஞ் சந்துபுற வடியும் வீங்கிச்

செய்கிதமாஞ் சிறுவிரல்கள் மிகவும் நொந்து

சிந்தைதரு மாறியே சலிப்புண் டாகும்"

பைகிதமாம் பைத்தியத்தில் வாத மிஞ்சிப்

பாரமாய் உற்பவித்து அழலுண்டாகும்

உய்கிதமாய் அசனமது தானும் வேண்டா

உதிரவாத சுரோணிதத் துணர்ச்சி யாமே

பொருள்

- கணுக்கால், முழங்கால், சந்துகள் இவைகளில் வீங்கும. Swelling in ankle joint, knee joint, dorsum of foot and other joints
- அழல் உண்டாகும் (Increased pitham)
- பசியின்மை உண்டாகும் (Loss of appetite)
- சிறுவிரல்கள் மிகவும் நோயை (Pain) பிறப்பிக்கும். (Pain in fingers that is interphalangeal joints)
- சிந்தை தடுமாறும் (Mental confusion)
- சலிப்புண்டாகும் (Easy fatiguability

In Pararasasegaram,

"பொர்சீதே வுதிர வாத சுரோணித முழங்கால் தானும்

பொற்கணைக் காலும் சந்தும் புறவடி தானும் வீங்கி

நற்கணு விரல்க ளொந்து நடுப் பயித்திய வாதத்தில்

உற்பவக் குணமுமுண்டா முறுநூலிற் சொன்ன தாமே"

உதிரவாத சுரோணிதத்தில்

1. முழங்கால், கணுக்கால், சந்துகள், புறவடி (Dorsum of foot) ஆகிய இடங்களில் வீங்கும்
2. கணுக்காளில் உள்ள விரல்கள் தோறும் வலியுண்டாகும் (Pain in metacarpophlangeal and interphalangeal joints)
3. பயித்திய வாதத்தில் காணும் குணங்கள் உண்டாகும் (Osteoporosis)

factors stimulating vatha disease

"தொழில் பெறுகைப்புக் கார்த்தல் தவர்த்தல் விசுகினு சோறும்

பழைய தாம்வரகு மற்றைப் பைந்தினையருந்தினாலும்

எழில் பெறப் பகலுறங்கி இரவினிலுறங் காதலாலும்

பிழை நிகர் குரலினாலே வாதங் கோபிக்குங் காணே"

- ❖ Intake of items excessive in bitter and astringent taste.
- ❖ Intake of old cooked food items
- ❖ Sleeping in the day time and awakening at night.

"காணவே மிகவுண்டாலும் கருதுபட்டினி விட்டாலும்

மானை யார்கண் மோகமறக்கினு மிகுந்திட்டாலும்

ஆணவ மலகடம் மையனே விடாதலாலும்

வானுதன் மடநல்லாளே வாதங் கோபிக்கும் கானே"

- ❖ Excessive intake of food
- ❖ Starvation
- ❖ Excessive sexual desire

"பாரினிற் பயப்பட்டாலும் பலருடன் கோபித்தாலும்

காரெனக் கருதியோடிக் கழுமரத்துரத்தினாலும்

ஏர்பெறு தனது ரெசின் மிகத்துக்க மடைந்திட்டாலும்

பாரிய காற்றினாலும் படரினும் வாதங் காணும்".

- ❖ Fear
- ❖ Anger
- ❖ Excessive running
- ❖ Stress
- ❖ Exposure to wind daily

"காலங்கண் மாறியுண்ணும் காரியக் தாலுந்தண்ணீர்

சாலவே யருந்தினாலும் சந்தியிலுட் கார்ந்தாலும்

கோலமாம் புளிப்பு நெய்மை குறைவற வருந்தினாலும்

வாலவார் முலைநல்லானே வாதமுற் பலிக்குங் காணே"

- ***யூகி வைத்திய சிந்தாமணி***

குளிர் காற்றில் உட்கார்ந்திருத்தல், புளிப்பு, நெய் உணவில் மிகுதியாக சேர்த்து கொள்ளல், காலம் தவறி உண்ணல் ஆகிய காரணங்களினால் வாதம் தோன்றும்.

"காணவே மிகவுண்டாலுங் கருதுபட்டினி விட்டலும்

மானனை யார்கண் மோகமிறக்கினு மிகுந்திட்டாலும்

ஆணவ மலங்கடமை யங்ஙனே விடாததாலும்

வானுதன் மடநல்லாளே வாதங்கோ பிக்குங்காணே"

அதிக அளவு உண்ணல், பட்டினி கிடத்தல், ஆணவம் அதிகரித்தல் ஆகியவற்றால் வாதநோய்கள் தோன்றும்.

"வளி தரு காய்கிழங்கு வரைவிலா தயிலல் கோழை

முளி தயிர் போன்மிகுக்கு முறையிலா வுண்டி கோடல்

குளிர்தரு வளியிற் றேகங் குனிப்புற வுலவல் பெண்டிர்

குளித்தரு முயக்கம் பெற்றோர் கடி செயல் கருவியாமால்"

- ***சபாபதி கையேடு***

EXTRINSIC FACTOR

- Exposure to dampness and cold
- Sleeping during day time
- Month from aani to karthigai

INTRINSIC FACTOR

- Intake of old cooked food
- Drinking rain water
- Intake of food items which excess in bitter,astringent,and pungent taste

SIDDHA PATHOLOGY

Siddha system of medicine is based on Thirithodam theory. They are vatham, pitham and kapham the manifestation of all diseases are result of derangement of these uyir thathus (Thirithodam)

When the seven thathu and mukkutram are in equilibrium, a normal structural and physiological state of body is ensured.As the thathu are affected by the extrinsic and intrinsic causative factors there will be distortion in the structural and functional state of the body.

; In Uthiravatha suronitham

1. Vatham – increased

"வாதமலாது மேனிகெடாது"

Different kinds of vatham

1. Uyir kaal – Praanan (Respiratory functions)

"..... நலமான குணமெல்லாம் பிராண வாயு
பன்னவே நீலவண்ணம் தெய்வம் சந்திரன்
பலப்பலவாம் பொசிப்பெல்லாம் சீரணமாகும்.

\- *யூகி முனிவர்*

This is the force of vital airs. According to Yugi muni, pranan starts from Moolatharam and comes through the nostril and dose inspiration and expiration. The inspiration and expiration is not uniform as the ratio is 8:12 there by the process of respiration is not complete. The praana helps in the digestion of ingested food.

2. **Keel Nokku Kaal – Abanan (Excretory funtion)**

"..... மருக்கவே கீழ்நோக்கி மலசலந்தள்ளும்
வாகாக நிறந்தானும் பச்சை யாகம்
அருக்கவே யாசனத்தைச் சுருக்கி வைக்கு....."

Abanan, the downward air, starts from swathittanam and descends down and is responsible for excretion of urine and faeces. It contracts the anus. It helps to take the essence of the digested food to the different parts of the body.

3. Vyaanan (Perfusion of oxygen nutrients)

"தறுப்பான சரவசரந் தனிலே நின்று

தானீட்டால் முடக்கல் பண்ணிப் பரிசமறியும்

அறுப்பான வன்னசா ரந்தன் னைத்தான் ....."

Vyaanan arises from the shoulders and go through all the 72,000 nerves and thus activate voluntary and involuntary movements of the body and thus make them to extend or contract. This appreciates the sense of touch, helps to take the essence of the food to the strategic points of the body and guards the body.

4. Udhaanan (Reverse peristalsis)

It is responsible for the physiological reflex actions like vomiting , hiccup, cough etc.,

5. Samaanan (Homestatic functions)

".....வாமென்ற வாயுவின் மிஞ்சொட்டாமல்

மடக்கியே சமன்செய்து மருவப் பண்ணும்

தாமென்ற அறுசுவையைத் தண்ணீர் ரன்னம்

சமன் செய்து சரீரமெலாஞ் சாரப்பணும்....."

Samaanan starts from the umblical cord and spread out upto the lower limb. This is responsible for the balance of the other four vathas. It equalises the six tastes, water, food etc. and helps in assimilation.

6. Naakan (higher intellectual functions)

It is responsible for the intelligence of an individual waking, singing and pilo erection.

7. Koorman (Constrictory functions)

It is responsible for yawning, closing of mouth winking, shedding of tears, vision and opening of the eyes.

8. Kirukaran (secretory functions)

"..... கசிவுண்டாங் கடும்பசியிற் கன்மஞ் செல்லும்

கண்ணியே யிருத்தலொடு போத லாகும்

துசிவுண்டாய்த் தும்மலோ டிரும லுண்டாம்..."

Kirukaran lies in the tongue and causes nasal and salivary secretions. It induces hunger, it makes to concentrate one thing, sneezing and cough are attributed to kirukaran.

9. Devathatan (Mental and physical sluggishness)

It is responsible for laziness, quarrelling, arguing.

10. Dhananjayan (Bloater of the body)

It leaves the body by blowing up the cranium only on the third day after death.

In case of Uthiravatha suronitham

S.No.	Vatham	Affected
1.	Abanan	Constipation
2.	Vyaanan	Restricted joint movements
3.	Samaanan	Due to derangement of other vayus
4.	Kirukaran	Loss of appetite
5.	Dhevathatan	Insomnia

II. PITHAM

Types of Pitham

1. Anar pitham

Its action is characteristic of theyu. This is responsible for dryness and digestion of food.

2. Ranjaga pitham

It is responsible for the colour and contents of the blood.

3. Saathagam

It controls the whole body. It is responsible for the action what we think.

4. Aalosagam

It is responsible for the vision.

5. Prasagam

It is responsible for the vision.

In case of Uthiravatha suronitham

S.No.	Pitham	Affected
1.	Anal pitham	Loss of appetite
2.	Ranjaga pitham	Pallor due to low Hb
3.	Saathaga pitham	Difficulty in walking, climbing upstairs, squatting etc.
4.	Prasaka pitham	Skin pallor

III. KABHAM

Kapha has been further divided into five as follows.

1. Avalambagam

Lies in lungs, controls the heart and other kabhas.

2. Kilethegam

Lies in stomach, makes food soft and helps in digestion.

3.Pothagam

Responsible for identifying tastes.

4. Tharpagam

Present in the head and responsible for the coolness of both eyes.

5. Santhigam

It lies in the joints and responsible for the action of joints. The above function may be altered whatever the mukkutram is altered.

In case of uthiravatha suronitham

S.No.	**Kabam**	**Affected**
1.	Klethagam	Loss of appetite
2.	Santhigam	Restricted movements of joints.

PINIYARI MURAIGAL (METHOD OF DIAGNOSIS):

It is based upon three main principles.

i) Poriyal Arithal (Inspection)

ii) Pulanal Arithal (Palpation)

iii) Vinaathal Arithal (Interrogation)

i) Poriyal Arithal

Pori means "Five Sense Organs"

1. Mei (Skin)
2. Vai (Tongue)
3. Kan (Eye)
4. Mookku (Nose)
5. Sevi (Ear)

ii) Pulanal Arithal

Pulan are five senses. They are,

1. Smell
2. Taste
3. Vision
4. Sensation of touch (palpation)
5. Hearing

"Pulanal Arithal" means examining the "Pulan" of the patient by the "Pulan" physician to diagnose a disease.

iii) Vinaathal Arithal

Vinaathal is collect the information the history of disease, its clinical features etc, from the patient or his / her close relatives useful when the patient is unable to speak or in the case of a child.

DIAGNOSTIC METHODOLOGY IN SIDDHA SYSTEM OF MEDICINE

ENVAGAI THERVUGAL (EIGHT DIAGNOSTIC TOOLS)

These Tools not only help in the diagnosis but also helps to observe the prognosis of the diseases and for reassuring the patient and to be informed about the nature of diseases, they are

1. Naadi (Pulse)
2. Sparisam (Sensation to Touch)
3. Naa (Tongue)
4. Niram (Colour)
5. Mozhi (Voice)
6. Vizhi (Eyes)
7. Malam (Faeces)
8. Moothiram (Urine)

Naadi (Pulse)

The study of 'Naadi' is the important diagnostic stool in Envagai thervugal which gives almost the correct diagnosis. This method developed by siddhars to extend our sensual perceptions to the interior of our body to diagnose and confirm illnesses. The study of naadi at hand is the best because the radial artery is located superficially, the unique factor which pertaining the soul in the body is known as "Naadi". Naadi is felt in right hand for males and left hand for females. It is usually felt using 3 fingers (viz index, middle and ring fingers) in view of assessing the states of vatham, pitham, kabham in the ratio of 1: ½ : ¼ normally. Derangement of this ratio leads to various disease.

"கரி முகனடியை வாழ்த்தி

கைதனில் நாடி பார்க்கில்

பெருவிரலங் குலத்தில்

பிடித்தடி நடுவே தொட்டால்

ஒரு விரலோடில் வாதம்

உயர் நடு விரலில் பித்தம்

திரு விரல் மூன்றிலோடில்

திரு விரல் மூன்றிலோடில்

சிலேத்தும நாடி தானே"

- *அகத்தியர் -2000*

In Uthira vatha Suronitham, vatha kalappu Naadi will be felt.

Vadha Naadi

"வாதமெனும் நாடியது தோன்றில்

சீதமந்தமொடு வயிறு பொருமல் திரட்சிவாய்வு

சீதமுறுங் கிராணி மகோதரம் நீராமை

திரள்வாய்வு சூலை வலிகடுப்புத் தீர

நீரமுறுங் கிருமிகுன்மம் அண்டவாதம்

நிலையும் நீர்க்கிரிச்சரங்கள் தந்து மேகம்

பேதகமா முதரப்பிணி மூல ரோகம்

பேசவெகு பிணிகளுமே பொருள தாமே"

- *சதக நாடி*

Vatha Pitha Naadi

"பொருளான வாதத்தில் பித்தஞ் சேர்ந்து

பொருந்து குணங்களா முஷ்ணவாயு சக்தி

செரியாமை புளித்தேப்பம் பொருமல் நிரிற்

சிவப்புமலம் பிடித்தலுருந் தாது நட்டம்

கருவான தேகமதி லுளைச்சல் சோம்பல்

கைகால் தறிப்புநாக் கசக்கு மன்னம்

பரிவான ஊண்குறைதல் ருசிகே டாதல்

பலநோயும் வருத்திவைக்கும் பாங்கு தானே"

- *சதகநாடி*

2. **Sparism (Palpation)**

Skin examination reveals about the warmthness/chillness , dry/weeping skin, rough/smooth, soft/hard, tenderness, presence of ulcers, fissures, swelling, wrinkle, hair pigmentation etc.

In Udhira vatha suronitham the affected part may feel warm with swelling and tenderness.

3. Naa (Tongue)

The colour changes according to changes in Mukkuttram, coated tongue, dryness, Jaundice, cyanosis, paleness, ulcer, peeling of skin, fissures, teeth marks in the border, tumours, taste, deviation of the tongue and excessive salivation should be noted.

In Udhira vatha suronitham the tongue may be dry and coated. If anamia is present, the tongue may be pale.

4. Niram (colour)

By the examination of niram, the type of dhegam (body) cyanosis, redness, pallor, yellow discolouration can be noted.

Vatha Dhegi - Dark colour

Pitha Dhegi - Yellow or red colour

Kabha Dhegi - White or yellow colour

5. Mozhi (Speach or voice)

In the examination of mozhi, the pitch of voice (low or high) action of laughing, crying, slurring and speech in hallucination can be noted.

6. Vizhi (Eye)

Changes according to mukkutram, redness of eyes, ulcers, other diseased conditions should be noted.

7. Malam (Stools)

Vatha type : Black colour, stools with constipation.

Pitha type : Loose stools with yellowish red colour

Kapha type : White coloured stools with muccus

Thontha type : Stools possess some of the features of two doshas.

Other examinations like diarrhoea, presence of blood, ova, cyst odour should be noted.

In uthira vatha suronitham constipation may be present.

8. Moothiram (Urine)

The examination of urine is classified into two types

1. Neer kuri
2. Nei kuri

1. Neerkuri

- ❖ Niram indicates the colour of the urine
- ❖ Edai indicates the specific gravity of urine
- ❖ Manam indicates the smell of the urine
- ❖ Nurai indicates the frothy nature of the urine
- ❖ Enjal indicates the quantity (increasd or decreased) and deposits of urine voided.

In addition, frequency of micturition and sediments are noted.

2. Neikuri

"அருந்து மாறிரதமும் அவிரோத மதாய்
அ:கல் அலர்தல் அகால வுண் தவிர்ந்தழற்
குற்றள வருந்தி உறங்கி வைகறை
ஆடிக் கலசத் தாவியே காதுபெய்
தொரு முகூர்த்த கலைக்குட் படுநீரின்
நிறக்குறி நெய்க்குறி நிருபித்தல் கடனே"

- *தேரையர்*

Procedure

Prior to the day of urine examination for neikuri, the patient is advised to take a balanced diet and the quantity of food must be proportionate to his appetite. The patient should have a

good sleep. After waking up in the morning the first voided urine is collected in a glass container and is subjected to analysis withing one and half hours.

A drop of gingelly oil is dropped over urine without disturbing the nature of the neikuri should be noticed in direct sunlight. The spreading pattern exhibited by the oil droplet over the surface of urine gives a confirmatory clue that helps in the disease.

SEVEN UDAL THATHUKKAL

1.	Saaram	Strengths the body and mind.
2.	Senneer	Gives power, knowledge and boldness to the mankind.
3.	Oon	It strengthens the body.
4.	Kozhuppu	It lubricates the joints.
5.	Enbu	It protects all the internal organs and gives the structure to the body.
6.	Moolai	It is present in the bone marrow
7.	Sukkilam and Suronitam	Reproduction

S.No.	**Udal kattukal**	**Decreased features**	**Increased features**
1.	Saaram	Loss of weight, lassitude, Dryness of the skin, Diminished activity of sense organs	Leads to disease identical to increased kabham, like loss of appetite, profuse salivation, depression etc.
2.	Senneer	Tiredness, Lassitude, Anaemia, Dryness	Increased blood pressure Reddish eye and skin jaundice, Haematuria, Boils and tumors in different parts of the body.
3.	Oon	Muscle wasting, lethargic sense organs	Extra growth around neck, face, abdomen, thigh, genitalia etc.
4.	Kozhuppu	Joint pain, Emaciation,	It leads to identical features of

		Splenomegaly.	increase oon associated with dyspnoea on exertion
5.	Enbu	Joint pain, falling of teeth, splitting and falling of hair and nails.	Excessive ossification and dentition.
6.	Moolai	Osteoporosis of the bone, blurred vision.	Obesity, swelling of interphalangeal joints, oliguria, Non-healing ulcers.
7.	Sukkilam (or) Suronitham	Pain in the genitalia failure to reproduce	Increased sexual activity , Increased formation of urinary calculi.

In uthiravatha suronitham saaram, seneer, oon, kozhuppu, enbu are commonly affected.

TYPES OF VATHA SURONITHAM IN YUGI CYINTHAMANI

- Vadha Suronitham
- Sithuvatha Suronitham
- Vaithiya Vatha Suronitham
- Paithiya Vatha Suronitham
- Slethumavatha Suronitham
- Utharavatha Suronitham
- Uthiravatha Suronitham

சித்துவாதசுரோணிதம்

“வாறான சரீரமெல்லா நுழைந்து ஊதல்
மாசற்ற தோல்தானுந் திரைந்து போகும்
நாறான நாறுபோல்ந ரம்பு சுக்கும்
நாக்குத்தான் வழவழத்துக் கோழை யாகும்
நூறான நெருப்புத்தான் பட்டாற் போல
நொந்துமே சடமெல்லாம் கொப்ப ளிக்கும்

வீறான வுரிந்துபின்னை வெதும்பி வீங்கும்

மிக்கசித் துவாதசுரோ ணிதம தாமே".

SITHUVATHA SURONITHAM

- Anasarca.
- Wrinkles.
- Neural pain.
- Glossy tongue.
- Sialorrhoea.
- Bullous eruption as in burn.
- Exfoliation, swelling and Warmthness.

சேத்துமவாதசுரோணிம்

"பண்பாக வுடல்குளிர்ந்து ஏறு வீங்கிப்

பதைப்பான விடந்தொட்டாற் பார நோவாம்

திண்பான சிரசுநெற்றி நோக்கா டுண்டாம்

சிலேட்டு மமாய்க்கோழை யொடுசு வாசமாகும்

மண்பாக மயக்க மொடு கனவு முண்டாம்

வாய்வரண்டு ருசியில்லா வருத்த மாகும்

நண்பாக நாடியுமே பட படக்கும்

நற்சேட்ப சுரோணிதமாம் நாடுங் காலே".

SLETHUMAVATHA SURONITHAM

- Chillness with abdominal distension.
- Severe pain and Head ache.
- Syncope and Hallucination.
- Dryness of mouth and Anorexia.
- Tachycardia.

உதரவாதசுரோணிதம்

"நாடுமே சுரம்வந்து நடுக்க லுண்டாம்
நாவரண்டு தலைநொந்து உடம்ப ழுத்தி
வாடுமே தேகமெல்லா மனிச்சப் பூப்போல்
மகாவருத்த முண்டாகி மயக்க மாகும்
சாடுமே யடிக்கடிதான் பேதி தானும்
தவிக்குமே தண்ணீர்தா னாட்ட மாகித்
தேடுமே சோற்றின்மேல் நினைவு தானும்
செயவுதர வாதசுரோணி தந்தா னென்னே".

UTHARAVATHA SURONITHAM

- Fever with rigor.
- Dryness of mouth.
- Pain in all over the joints.
- Headache.
- Diarrhoea.
- Excessive thirst.
- Hunger.

வைகிதவாதம்

"ஆமென்ற வீங்கினதோர் விடத்தில் ரத்தம்
அழுத்தமாய்த் திரண்டுமே எங்கும் பாய்ந்து
ஓமென்று ஓட்டியேதி ரண்டி ருக்கும்
உறுதியாய்த் தொட்டுடனே மெத்தென் றாகும்
தேமென்ற தேகமெங்க ணுமு சுக்கும்
சீறிய தோரிருமலொடு காச்ச லுண்டாம்
பாமென்ற படந்தனிலே திமிருண் டாகும்
பாரமாய் வைகிதமாம் வாதந் தானே".

- யூகி வைத்திய சிந்தாமணி

Uthiravatha Suronitham is differentiated from other types of Vatha Suronitham as follows:

VAIKITHA VATHA SURONITHAM

- Swelling with hyperaemia.
- Soft on touch.
- Cough with pyrexia.

  Irritability.

வைகிதவாதம்

“ஆமென்ற வீங்கினதோர் விடத்தில் ரத்தம்
அழுத்தமாய்த் திரண்டுமே எங்கும் பாய்ந்து
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- Irritability.

SIRAPPU MARUTHUVAM FOR VATHA DISEASE

1. ஒற்றடம்
2. வேது
3. தொக்கணம்

4. ஆசனம்
5. பிராணாயாமம்
6. தியானம்

SPESIFIC TREATMENT FOR UTHIRA VATHA SURONITHAM

வேது (STEAM BATH) :

- உடலிருந்து வியர்வை பெருகும்படி செய்வதற்கு ஏற்றமுறைகளில் ஒன்று வேது.
- நீரைச் சில மூலிகைகளுடன் சேர்த்து கொதிக்க வைத்து அதனின்று எழும் ஆவியை பிடித்தல்.

A steam room is an enclosed space with large amounts of high temperature steam, creating a high humidity environment. People sit in this room in a similar way to a sauna (conversely a hot, but dry atmosphere), for relaxation and purported benefits to health and well being. Steam rooms are commonly maintained at a temperature of 41 degrees Celsius or above, with a high humidity of around 100% adding to the sensation.

The benefits of a steam bath are numerous. Some of the benefits include:

- The most common and obvious reason is to relieve tension buildup and various forms of stress.
- Various ailments such as arthritis, muscle pains and the like can be relieved because of its warm effect to the body.
- Old people will surely benefit from this since joint pains and other body pains can be relieve.
- Steam rooms due to its heat effect make you sweat a lot thus your body will eventually release toxins and other negative energies.
- It will also regulate and stimulate the flow of your blood and make your metabolism works faster.
- It also makes your skin looks fresh, young looking and truly healthy.
- It can give you a lot of self-confidence due to the good effects it will cause to your personal appearance.
- Increases circulation for healthier skin & more energy.
- Relaxes stiff muscles & ceases swelling or tension in joints associated with arthirits.

- As well as nutrients also gets pushed to the surface of the skin, which may have a positive effect on collagen production. Collagen makes bones stronger and helps cell regeneration. That part about cell regeneration makes it partially accountable for firmer skin.

Anyone suffering from sleeping disorders, poor skin circulation & Muscular tension & Weakness will benefit from taking a steam bath.

பிராணாயாமம் (BREATHING EXERCISE)

பிராண வாயுவின் அசைவு எதுவோ அதுவே, சித்தத்தின் அசைவென்றும் பிராண வாயுவின் சலனத்தை வென்றால் சித்தத்தை வயப்படுத்தலாம் எனவும், கூறப்படுகிறது

Benefits of Pranayamam

- பிராணாயாமத்தினால் சர ஓட்டம் சீராக்கப்பட்டு அதன் மூலம் வளி, அழல், ஐயம் ஆகிய மூன்று உயிர்த்தாதுக்களும் சமநிலையில் நடக்கும். மூன்று உயிர்தாதுக்களும் சீரடையும் போது நோய்களும் கட்டுப்படும். அதேபோல் உதிரவாத சுரோணிதத்தில் பாதிப்படைந்த வளி, அழல் சமப்படுத்தப்படுகிறது.
- சுவாசத்திற்கும், மனதிற்கும் நெருங்கிய தொடர்பு இருப்பதால் உதிரவாத சுரோணிதத்தில் தோன்றும் மனசலிப்பு (Depression) நீங்கி, மனவலிமையும் (Self Confidence), நல்ல தூக்கமும் (Quite sleep) உண்டாகிறது.

- Improve health and heal diseases
- Improve concentration and mental focus
- Bestow joy, peace and happiness
- Bestow psychic powers and yoga siddhis
- Awaken, balance and heal the chakras
- Increase energy, vitality and awareness
- Cure insomnia and help break bad habits
- Help manifest desires and intentions
- Self-Realization.

தியானம் (MEDITATION)

இது அஷ்டாங்க யோகம் (அ) அகத்தத்துவம் எட்டு என்பனவற்றுள் ஒன்றாகும். தியானம் மூலம் ஆதாரங்கள் சீர்பட்டு நோய் நீக்கத்திற்கு மட்டுமின்றி நோய் வராமலும் தடுக்கலாம்.

உதிரவாத சுரோணிதத்தில் பெரும்பாலான நோயாளிகள் வருத்தம், சலிப்புடன் காணப்படுகின்றனர்.

நன்மைகள்

- தியானத்தின் போது செரடோனின் (Seratonin) சுரப்பு அதிகமாவதால் மனத்தெளிவு உண்டாகும்.
- Endorphin, Encephalin போன்ற சுரப்புகள் அதிகமாவதால் வலிகளிலிருந்து நிவாரணம் கிடைக்கிறது.

- It lowers oxygen consumption.
- It decreases respiratory rate.
- It increases blood flow and slows the heart rate.
- Leads to a deeper level of relaxation.
- Good for people with high blood pressure as it brings the B.P. to normal
- Reduces anxiety attacks by lowering the levels of blood lactate.
- Decreases muscle tension (any pain due to tension) and headaches.
- Builds self-confidence.
- It increases serotonin production which influences mood and behaviour. Low levels of serotonin are associated with depression, obesity, insomnia and headaches.
- Helps in chronic diseases like allergies, arthritis etc.
- Reduces Pre-menstrual Syndrome.
- Enhances the immune system. Research has revealed that meditation increases activity of ‘natural-killer cells’, which kill bacteria and cancer cells.

ஆசனங்கள் (YOGASANAM)

உதிரவாத சுரோணிதத்தில் பொதுவாக மேற்கொள்ளப்படும் ஆசனங்கள் கடினமின்றி இருத்தல் வேண்டும்.

Yogasanam

Several clinic and university studies have shown that yoga is an excellent and effective way to relieve arthritis symptoms. The British Journal of Rheumatology published a study in 1994 which showed arthritis symptoms improving in patients who practiced yoga. The Rheumatic Diseases Clinics of North America published two studies in 2002 which detailed the relief of joint stiffness and pain for those who regularly practice yoga.

Since rheumatoid arthritis is the result of the immune system damaging the joints, yoga provides even further benefits for those suffering from this type of arthritis. Practicing yoga helps balance all the body's systems, including its immune defences. Correcting immune system problems can greatly reduce the instance of pain related to rheumatoid arthritis.

Scientific studies in major medical journals have found that yoga can help arthritis patients by

- Building muscle strength
- Increasing flexibility
- Promoting better balance
- Reducing body aches and pains
- Creating a better sense of well-being
- Reducing feelings of anxiety and depression

ASANAM

MODERN ASPECT

Joints

The place of union or junction between two or more bones is called joint

Joints classified by

- Fibrous joints
- Cartilaginous joint
- Synoviyal joint
- General Classification of synovial joints
- Plane joint
- Hinge joint
- Pivot joint
- Bicondylor joint
- Saddle joint
- Elipsoid joint
- Saddle joint
- Ball and socket joints

JOINT	POSSIBLE MOVEMENTS
1. SHOULDER	Flexion & extension, adduction & abduction, circumduction, rotation
2. ELBOW	Flexion & Extension
3. RADIO-ULNAR	Pronation & Supination
4. WRIST	Flexion & extension, adduction & abduction, circumduction
5. SPINE	Flexion & extension, lateral extension, rotation.
6. HIP	Flexion & extension, adduction & abduction, circumduction.
7. KNEE	Flexion & Extension
8. ANKLE	Dorsi flexion & Plantar flexion

Features of a synovial joint

FEATURE	STRUCTURE	FUNCTION
Hyaline/articular cartilage	Smooth& spongy covers ends of bones	▪ Prevents friction between articulating bones
Two layered joint capsule	Outer layer – Tough & Fibrous Inner – Synovial membrane covers all internal surfaces	▪ To strengthen joint ▪ To secrete synovial fluid
Synovial fluid	Slippery fluid like egg white which fills joint capsule	▪ Reduce friction ▪ Nourish cartilage ▪ To get rid of waste from joint

RHEUMATOID ARTHRITIS

Definition

Rheumatoid arthritis is a chronic inflammatory autoimmune diaorder of human body. Its characterised by affecting the connective tissue of whole body with specific involvement of major and minor joints. that results in inflammation of joints, proliferative and destructive changes in synovial membrane, peri-articular structures, skeletal muscles and perineural sheaths.

EPIDEMIOLOGY

Eighty percent affected are women.

Male: Female ratio is 1:3

RA affects 0.5 to 1% of adults in the developed world

Aetiology

The cause remains unknown.

There is evidence of immune overactivity.

1. The presence in the serum of abnormal immuno globulin-rhematoid factors –IgG and IgM.
2. The infiltration of the synovial tissue by immunologically competent cells, lymphocytes, and plasma cells, which are responsible for the local production of immunoglobulins including rheumatoid factor.
3. The presence of immune antigen antibody complexes within leucocytes in synovial fluid and peripheral blood.
4. The finding of lowered complement levels in synovial fluid.

   It has been suggested that the basic mechanism in the production of the inflammation is the combination of rheumatoid factor and an altered immunoglobulin with the utilization of complement. The ingestion of the resulting immune complexes by neutrophils causes the release of lysosomal enzymes which act as a mediators of the synovitis (Weissmann, 1972). The alteration or production of the immunoglobulin with which rheumatoid factor combines is a vital step. If the alteration appears de novo, rheumatoid arthritis can be called an autoimmune disease.

Other aetiological factors

1. A genetic influence (DR4):

There is a tendency for the disease to be aggregated in families

2. Trauma

Many patients have mentioned traumatic incidents as a precipitating cause.

3. Psychological stress:

The study of identical twins in one of whom rheumatoid arthritis developed tends to support this concept (Meyerowitz et.al, 1968).

4. Infectious agents

Renewed interest in this subject has resulted in is isolation of a variety of organisms from synovial tissue, synovial fluid and blood. These include diphtheroid bacilli, mycoplasma and viruses.

5. Vascular changes

Alteration of the normal peripheral vascular bed, perhaps by autonomic influence, has been suggested as the primary abnormality. This has been implicated to explain the striking symmetry of the arthritis in many patients

AUTOIMMUNITY

Rheumatoid arthritis was classified as an autoimmune disease, cheifly following the discovery of IgM rheumatoid factor in the blood of the patients. The rheumatoid factor – secreting plasma cells have been demonstrated in the rheumatoid synovium, thus implicating them at the site of the disease

PATHOLOGY

The condition is widespread, but the brunt of the attack falls on synovium. The constant and characteristic feature is a chronic inflammation, an inconstant but pathognomonic lesion is the rheumatoid nodule.

Joints and tendons

The pathological changes, if unchecked, proceed in three stages.

Stage 1 Synovitis

Early changes are vascular congestion, proliferation of synoviocytes and infiltration of the subsynovial layers by polymorphs, lymphocytes and plasma cells. There is thickening of the capsular structure, villous formation of the synovium and a cell-rich effusion into the joints and

tendon sheaths. Though painful, swollen and tender these structures are still intact and mobile and the disorder is potentially reversible.

Stage 2: Destruction

Persistent inflammation causes joint and tendon destruction. Articular cartilage is eroded, partly by proteolytic enzymes, partly by vascular tissue in the folds of the synovial reflections and partly due to direct invasion of the cartilage by a pannus of granulation tissue creeping over the articular surface. At the margins of the joints, bone is eroded by granulation tissue invasion and osteoclastic resorption.

Similar changes occur in tendon sheaths, causing tenosynovitis, invasion of the collagen bundles and eventually, partial or complete rupture of tendons.

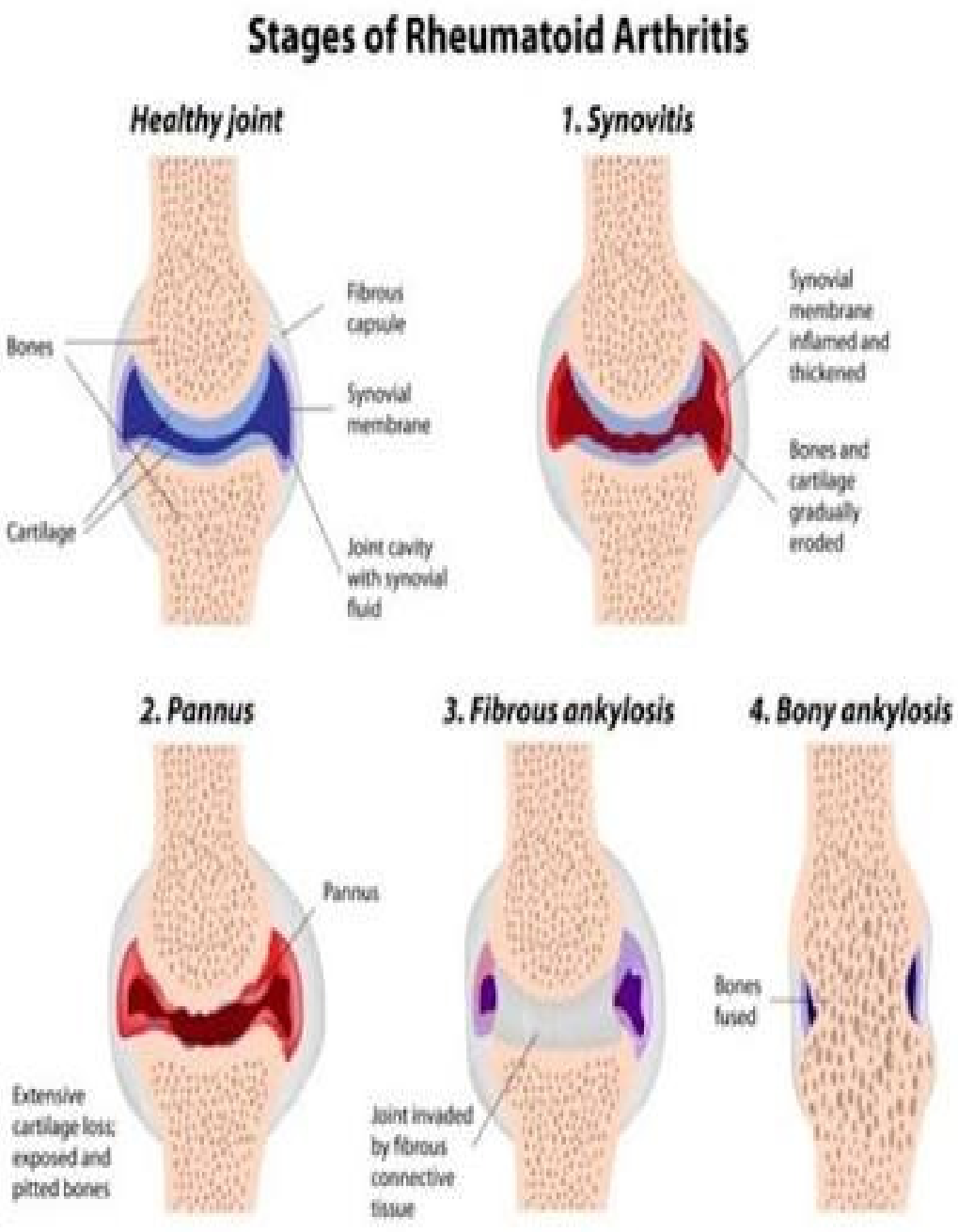
A synovial effusion, often containing copious amounts of fibrinoid material, produces swelling of the joints, tendons and bursae.

Stage 3: Deformity

The combination of articular destruction, capsular stretching and tendon rupture leads to progressive instability and deformity of the joints. By this times the inflammatory process may have subsided, the emphasis is now on the mechanical and functional effects of joint and tendon disruption.

True Rhematoid Nodule

Theses are occasionally formed in synoivial tissue and are diagnostic. They are more common in seropositive patients. The nodules may also be found in bursal and tendon sheaths. An arteritis is often found close to the nodule the center of the nodule shows fibrinoid necrosis, which is rimmed by palisading macrophages. The rheumatoid nodules develop and regress slowly and are less rich in hydroxyproline than the nodules of rheumatic fever.


Stages of Rheumatoid Arthritis
Healthy joint
Bones
Fibrous capsule
Synovial membrane
Cartilage
Joint cavity with synovial fluid
1. Synovitis
Synovial membrane inflamed and thickened
Bones and cartilage gradually eroded
2. Pannus
Pannus
Extensive cartilage loss; exposed and pitted bones
3. Fibrous ankylosis
Joint invaded by fibrous connective tissue
4. Bony ankylosis
Bones fused

CLINICAL FEATURES

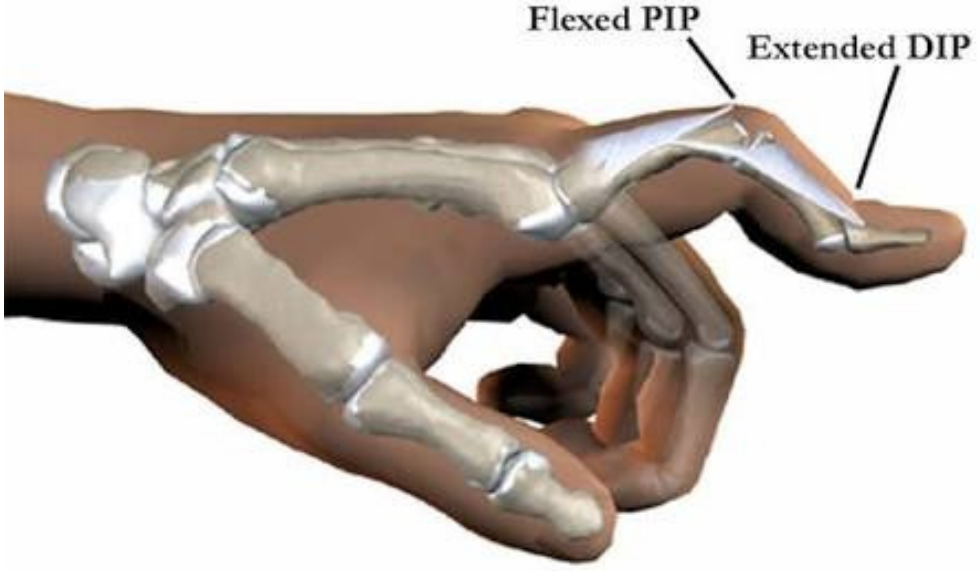
Onset

- Insidious onset with fatigue, malaise, anorexia, weakness and vague musculoskeletal symptoms, which are perhaps caused by cytokine such as interleukin-1 and tumor necrosis factor.
- Acute onset with rapid development of polyarthritis accompanied by constitutional symptoms including fever, lymphadenopathy and splenomegaly.
- Palindromic onset where recurrent acute episodes of joint pain and stiffness occur in individual joints lasting only a few hours or days.

Articular manifestations

- Joint involvement is usually symmetric. It is characterized by pain, swelling, tenderness and painful limitation of movements. The metacarpophalangeal and proximal interphalangeal joints of the hands, wrists, knees and the metatarsophalangeal and proximal interphalangeal joints of the feet are the most common joints involved.
- Generalised stiffness may occur but "morning stiffness" lasting more than 1 hour is a characteristic features. the intensity and duration of morning stiffnes is a measure of disease activity.
- Morning stiffness which is a reasonably specific symptoms of Rheumatoid arthritis is probably due to increase fluid in and around the joint. The proliferated and dilated synovial vessels cause the joint to feel warm and in fair skinned individuals a reddish discoloration of overlying skin may be observed.

Boutonniere Deformity




Rheumatoid arthritis
(late stage)
Boutonniere
deformity
of thumb
Ulnar deviation of
metacarpophalangeal
joints
Swan-neck deformity
of fingers
A.D.A.M.

Hand and wrist

- Swelling of the proximal but not the distal interphalangeal joints, results in "spindling" of the fingers.
- Hyperextension of the proximal interphalangeal joints with flexion of the distal interphalangeal joints results in "swan-neck" deformity.
- Flexion of the proximal interphalangeal joint and extension of the distal interphalangeal joints result in "boutonniere" or "button hole" deformity.
- Hyper extension of the first interphalangeal joint and flexion of the first metacarpophalangeal joint with a consequent loss of thumb mobility and pinch can occur.
- Extensor tendon rheumatoid granulomata and tendon rupture result in "dropped finger".
- Radial deviation of the wrist with ulnar deviation of the digits often with palmar subluxation of the proximal phalanges results in the "z" deformity.
- Wrist synovitis with median nerve entrapment can result in carpal tunnel syndrome.
- In the hand, the small joints are swollen and the fingers assume a position of "ulnar deviation".
- The fingers assume an "intrinsic plus deformity" which consists of flexion at the metacarpo phalangeal joints and extension at the interphalangeal joints.

Foot an ankle

- Swelling of the metatarso-phalangeal joints results in "broadening" of the forefoot.
- Lateral deviation and dorsal sub luxation of the toes.

EXTRA ARTICULAR MANIFESTATIONS.

Rheumatoid nodules

These develop in 25% of persons with RA. They are firm, round masses felt in the subcutaneous tissues-eg: the olecranon bursa, the proximal ulna, the Achilles tendon and the occiput. Visceral structure like heart, lungs and pleura may also be involved.

Rheumatoid nodules are clinical predictors of more severe arthritis, sero-positivity, joint erosions and rheumatoid vasculitis.

Pleuropulmonary manifestation

- Pleural involvement results in effusion with low levels of pleural fluid glucose (less than 10mg/dl)
- Pulmonary involvement resulting in interstitial fibrosis.
- Caplan's syndrome: multiple nodules and interstitial lung disease due to pneumoconiosis.

Cardiovascular manifestations

- Pericarditis and chronic constrictive pericarditis.
- Premature atherosclerosis (an important cause of increased morbidity and mortality)
- Valvular involvement
- Conduction defects

Neurological manifestations

- Nerve entrapement syndromes. Eg: carpal and tarsal tunnel syndrome.
- Spinal compression due to atlanto-axial subluxation.
- Peripheral neuropathies

Ophthalmological manifestations

- Scleritis, episclerits and scleromalacia perforans.

- ❖ Sicca complex. comprising keratoconjunctivits sicca, xerostomia and salivary gland enlargement.
- ❖ Glaucoma

Haematological manifestations.

- ➢ Normocytic normochromic anemia.
- ➢ Thrombocytosis
- ➢ Eosinophilia and mild leucocytosis.

- ➢ **Osteoporosis**

Osteoporosis secondary to rheumatoid involvement is very common. It may be aggravated by corticosteroid theraphy and immobilization

Felty's syndrome

This is the association of splenomegaly and neutropenia with RA

Management

- ❖ There is no cure for RA, but treatments can improve symptoms and slow the progress of the disease. Disease-modifying treatment has the best results when it is started early and aggressively.

- ❖ The goals of treatment are to minimize symptoms such as pain and swelling, to prevent bone deformity and to maintain day to day functioning.
- ❖ Need to make frequent assessments for the persons functional ability as the disease progress in order to provide realistic goals and support.

Dietary supplements

- ❖ Turmeric
- ❖ Cherries (6-8 cherries every day)
    - o High is magnesium natural pain killer
    - o Potassium – diuretic to reduce inflammation
- ❖ Omega – 3 polyunsaturated fatty acids (found in fish oil) is an effective treatment for RA.
- ❖ Two garlic pearls with 2 ounces of buttermilk is an excellent daily drink and home remedy for rheumatoid arthritis.
- ❖ Gamma-linolenic acid, which may reduce pain, tender joint count and stiffness is generally safe.

Prognosis

- ➢ The course of the disease varies greatly.
- ➢ Some people have mild short-term symptoms, but in most the disease is progresive for life.
- ➢ Around 20% - 30% will have subcutaneous nodules known as rheumatoid nodules. This is associated with a poor prognosis.

Classification criteria for Rheumatoid Arthritis (2010)

Features

A. Joint involvement *		**Score**
• One large joint **	-	0
• 2-10 large joints	-	1
• 1-3 small joints *** (with or without involvement of large joints)	-	2
• 4-10 small joints (with or without involvement of large joints)	-	3
• >10 joints (at least 1 small joint) ****	-	5

B. Serology (at least one test result in needed for classification)

• Negative RF negative anticitrullinated protein antibodies (ACPA)	-	0
• Low- positive RF or low-positive ACPA	-	2
• High – positive RF or high-positive ACPA	-	3

C.Acute – phase reactants (at least one test result is needed for classification)

• Normal CRP and normal ESR	-	0
• Abnormal CRP or abnormal ESR	-	1

D. Duration of symptoms

• < 6 weeks	-	0
• ≥ 6 weeks	-	1

- Add score of categories A-D, a score of ≥ 6/10 is needed for classification of a patient as having definite RA.

DIFFERENTIAL DIAGNOSIS

- Rheumatic Arthritis
- Psoriatic Arthritis

- Gouty Arthritis
- Osteo Arthritis
- Syphilitic Arthritis
- Ankylosing spondylosis

MATERIALS AND METHODS

The Study on Uthiravatha Suronitham was carried out in the OPD and IPD of the Sirappu Maruthuvam department, Govt. Siddha Medical College, Palayamkottai.

The trial drugs used are **Mathiyooshna Rasayanam** (Internal) indicated in the authorised Siddha text Yugimuni Vithyakaviyam (Page No.283) and **Nympathy thylam** (External) indicated in Sarabenthirar vaithiya Muraigal for Uthiravatha Suronitham.

Objectives:

Primary objective:

To evaluate the clinical efficacy of "**MATHIYOOSHNA RASAYANAM**" (internal) & "**NYMPATHY THAILAM"** (external) in reducing the pain and restricted joint movements in the treatment of **'Uthiravatha suronitham"** (rheumatoid arthritis).

Secondary objective:

To study the effect of Vedhu (steam bath) in reducing the pain towards the efficacy of medicine.

Study design & conduct of study:

Study type : Phase II Criteria based open clinical trial

Study place : OPD & IPD of Govt Siddha Medical College & Hospital, Palayamkottai

Study period : 24 months

Sample size : 40 patients (20 OP +20 IP). Out of 20 IP patients, 10 IP patients will be given Vedhu (steam bath) in addition to internal and external medicine and the remaining 10 IP patients will be given internal and external medicine.

Treatment:

Internal medicine: MATHIYOOSHNA RASAYANAM

Reference : Yoogimuni Vaithya Kaaviyam. Pg No: 283

Dose : Kottai paakku alavu(6.022 gm), twice a day.

Vehicle : Jaggery

Duration : 40 days

EXTERNAL MEDICINE: NYMPATHY THAILAM

Subject selections:

Patients reporting with symptoms of inclusion criteria in P.G. Dept of Sirappumaruthuvam, GSMC, Palayamkottai will be subjected to screening test and documented using screening proforma.

Inclusion criteria:

- Age : 18-60 years
- Sex : both male and female
- Symmetrical joint involvement
- Arthritis of 3 or more joints
- Rheumatoid factor positive or negative
- Morning stiffness
- Swelling especially in the inter phalangeal joint.
- Patients who are willing for admission and stay in IPD for 40 days or willing to attend OPD
- Patient who is willing to undergo radiological investigation and give blood and urine samples for laboratory investigation.
- Patient willing to sign the informed consent stating that he/she will consciously stick to the treatment during 40 days but can OPD out of the trial of his/her own conscious discretion.

Exclusion criteria:

- Systemic illness.
- Pregnancy and lactation
- History of trauma
- Neurological disorder

- Tubercular arthritis
- Any other serious illness
- Psoriatic arthritis
- Gouty arthritis

Withdrawal criteria:

- Intolerance to the drug and development of adverse reactions during drug trial.
- Poor patient compliance and defaulters.
- Patient turned unwilling to continue in the course of clinical trial.
- Occurrence of any adverse reactions.

Tests and assessment:

A. Clinical assessment
B. Routine investigations
C. Specific investigations
D. Radiological investigations
E. Siddha investigations

A. Clinical assessment:

- Arthritis involving three or more joints.
- Symmetrical joint involvement
- Morning stiffness
- Anorexia
- Spindle shaped appearance of fingers
- Rheumatoid nodules
- Depression
- Distaste to food
- Swelling of small joints of hands and foot.

B. Routine investigation:

Blood

Hb

Total WBC count

DC –

1. Polymorphs

1. Lymphocytes
2. Eosinophils
3. Monocytes
4. Basophils

Total RBC count

ESR

½ hr

1 hr

Blood sugar

r:

f:

pp:

Serum cholesterol.

Urine

Albumin

Sugar

Deposit

C. Specific investigations

CRP

RA factor

ASO titer

D. Radiological investigations:

X ray of affected joints (AP and lateral view)

E. Investigation based on siddha system:

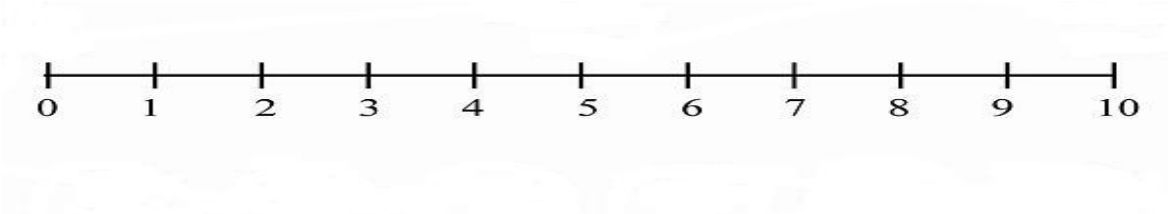
1. Naa
2. Niram
3. Mozhi
4. Vizhi
5. Naadi
6. Sparisam
7. Malam
8. Moothiram

Conduct of the study:

15ml of moolakudori ennai is given in early morning, on the very first day of treatment for purgation. This will help to bring the vitiated mukkutram back to normal. From the next day, the trial drug is given for treatment.

Then the trial drug **MATHIYOOSHNA RASAYANAM** (internal), **NYMPATHY THAILAM** (external) is given continuously for 40 days. OP patients should visit the hospital once in days. At each clinical visit clinical assessment is done and prognosis is noted. For IP patients the drug is given for 40 days and the clinical assessment is done daily. 10 IP patients will be given Vedhu (steam bath) treatment along with their internal medicine. The remaining 10 IP patients will not be given Vedhu (steam bath). The results will be compared at the end of the study. Laboratory investigations & radiological investigation are done 0 day, 20^{th} day, 40^{th} day of the trial. For IP patients, who are not in a situation to stay in the hospital for a long time (minimum 15 days in IPD remaining days are followed in OPD) is advised to attend the OPD for further follow-up. After the end of the treatment, the patient is advised to visit the OPD for another 2 months for follow-up. If any trial patient who fails to collect the trial drug on the prescribed day but wants to continue in the trial from the next day , he/she will be allowed, but defaulters of one week and more will not be allowed to continue and be withdrawn from the study with a fresh case being included.

Outcome:



The outcome is aimed at reducing the pain and weakness.

Universal pain assessment scale

A. 0 : no pain

B. 1 -3 : mild pain

C.4-6 :moderatepain

D.7-10 :severepain

Reference: clinical manual for nursing practice. (National institute of health warren grant magnuson clinical center)

Restricted movements is assessed by

Gradation of restricted movements:

- G i – able to perform normal duties
- G ii – moderate restriction – self care is possible.
- G iii – marked restriction – limited self care / some assistance required.
- G iv – confined to bed or wheel chair.

Adverse effect/serious effect management

If the trial patient develops any adverse reaction, he/she would be immediately withdrawn from the trial and proper management will be given in OPD of Govt. Siddha medical college and hospital, Palayamkottai.

RESULTS AND OBSERVATION

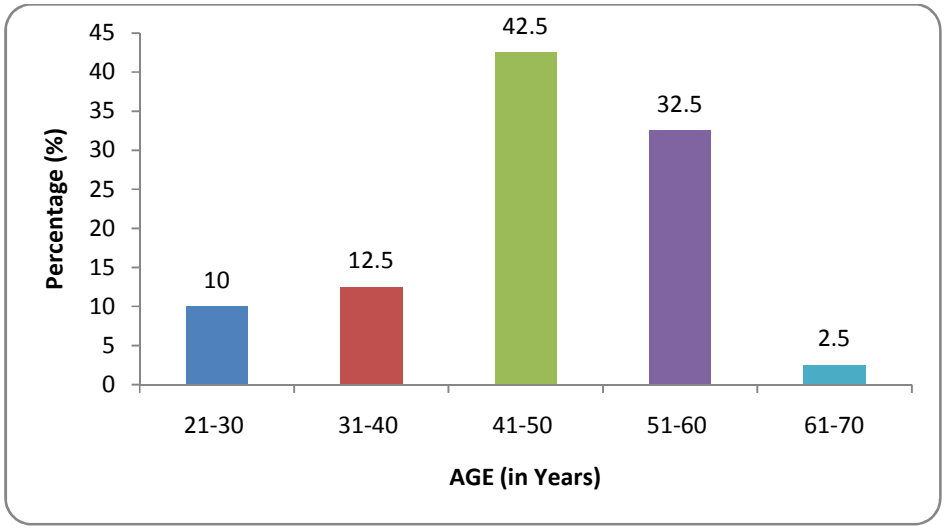
Results and observation are tabulated under the following headings,

1. Age distribution
2. Sex distribution
3. Religion
4. Body constitution
5. Paruva kaalam
6. Nilam
7. Diet
8. Occupational Distribution
9. Duration of Illness
10. Onset of symptoms
    a. Derangement in vatham
    b. Derangement in Pitham
    c. Derangement in kabam
11. Gnanenthiriyam
12. Udal thathukkal
13. Envagai thervugal
    A. Naadi
    B. Neikuri
14. Clinical features
15. Deformities
16. Involvement of joints
17. Results.

1. AGE DISTRIBUTION

Table 1

S.No	Age(years)	No of Cases	Percentage
1	21-30	4	10
2.	31-40	5	12.5
3	41-50	17	42.5
4.	51-60	13	32.5
5.	61-70	1	2.5
	Total	40	100



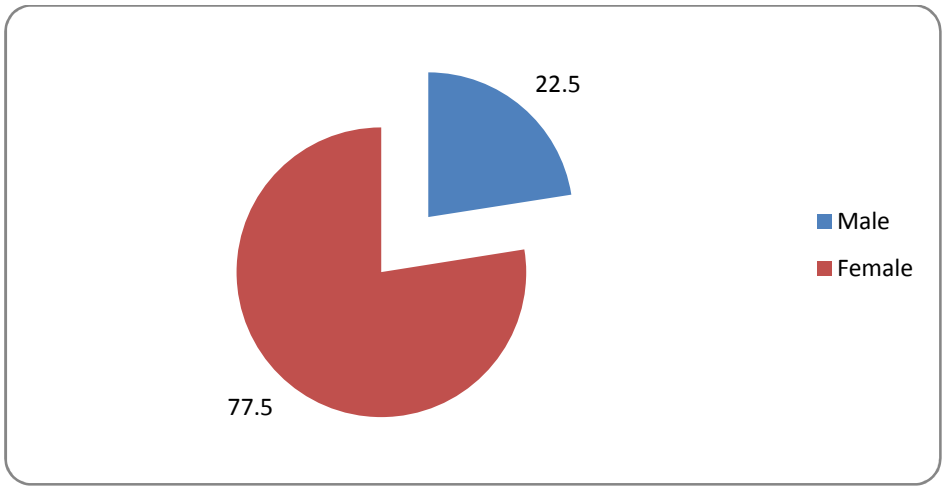
Inference

The percentage of age group is 41-50 years was 42.5%, 51-60 years was 32.5%, 31-40 years was 12.5%, 61-70 years was 2.5%, 21-30 years was 10%.

2. SEX DISTRIBUTION

Table 2

S.No	Sex	No of Cases	Percentage
1	Male	9	22.5
2.	Female	31	77.5
	Total	40	100



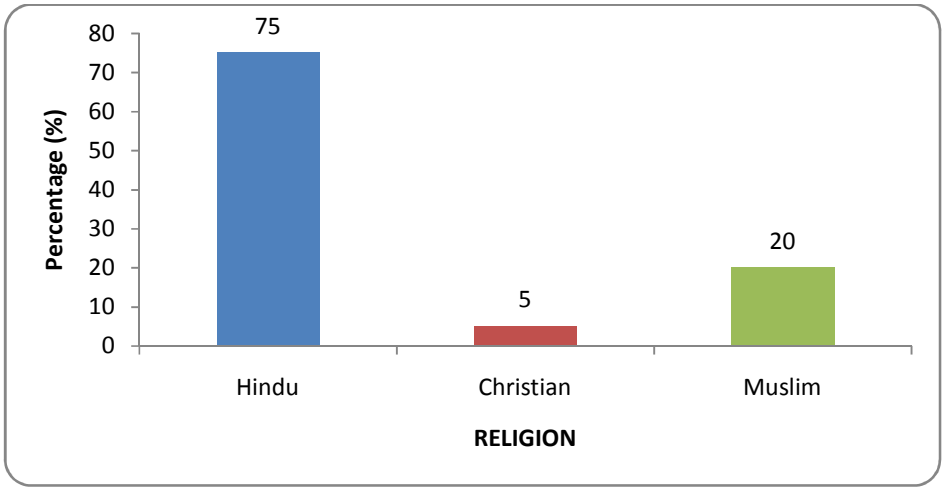
Inference

Among the patient selected 77.5% female were affected. 22.5% male were affected.

3. **RELIGION DISTRIBUTION**

Table 3

S.No	Reliion	No of Cases	Percentage
1	Hindu	30	75
2.	Christian	2	5
3.	Muslim	8	20
	Total	40	100



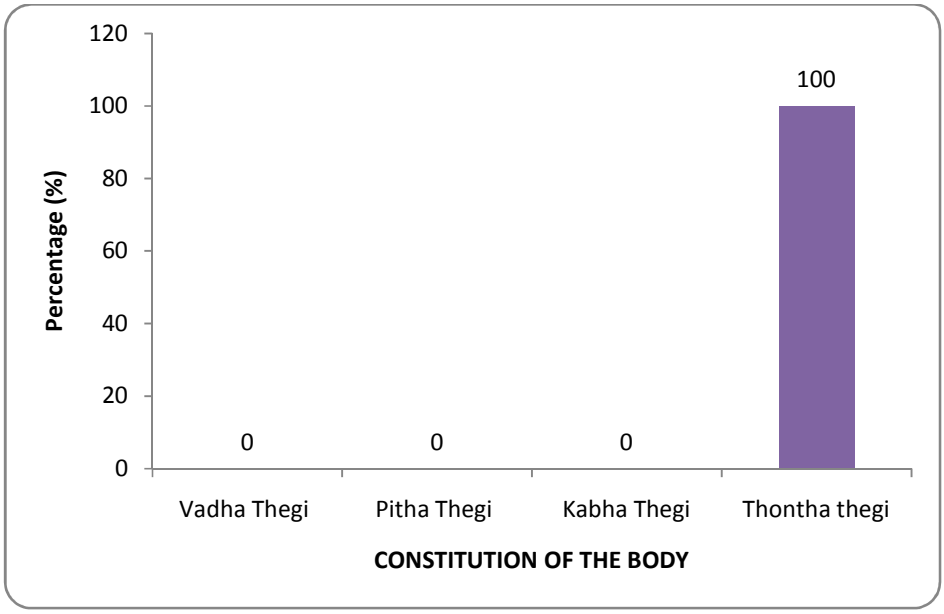
Inference

Among the 40 cases, 75% of cases belongs to hindhu and 20% cases belong to muslim and 5% cases belongs to christian.

4. BODY CONSTITUTION

Table : 4

S.No	Constitution of the Body	No of Cases	Percentage
1	Vadha Thegi	0	0
2.	Pitha Thegi	0	0
3.	Kabha Thegi	0	0
4.	Thontha thegi	40	100
	Total	20	100



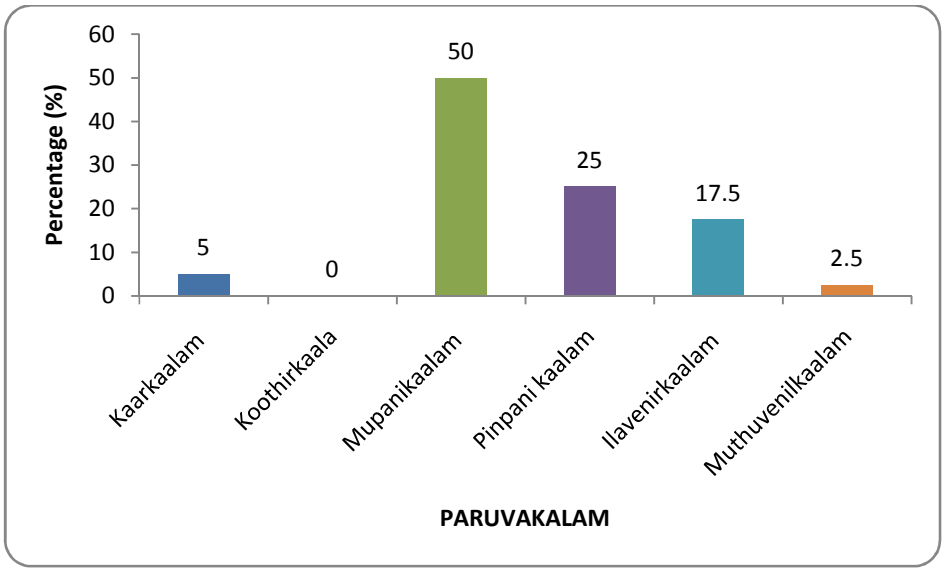
Inference

All cases were Thontha thegam.

5. PARUVAKAALAM

Table : 5

S.No	Paruvakaalam	No of Cases	Percentage (%)
1	Kaarkaalam (Aug 15- Oct 14)	2	5
2.	Koothirkaalam (Oct 15- Dec 14)	0	0
3.	Munpanikaalam (Dec 15 – Feb 14)	20	50
4.	Pinpani kaalam (Feb 15 – Apr 14)	10	25
5.	Ilavenirkaalam (Apr 15-Jun 14)	7	17.5
6.	Muthuvenilkaalam – (Jun 15 – Aug 14)	1	2.5
	Total	40	100



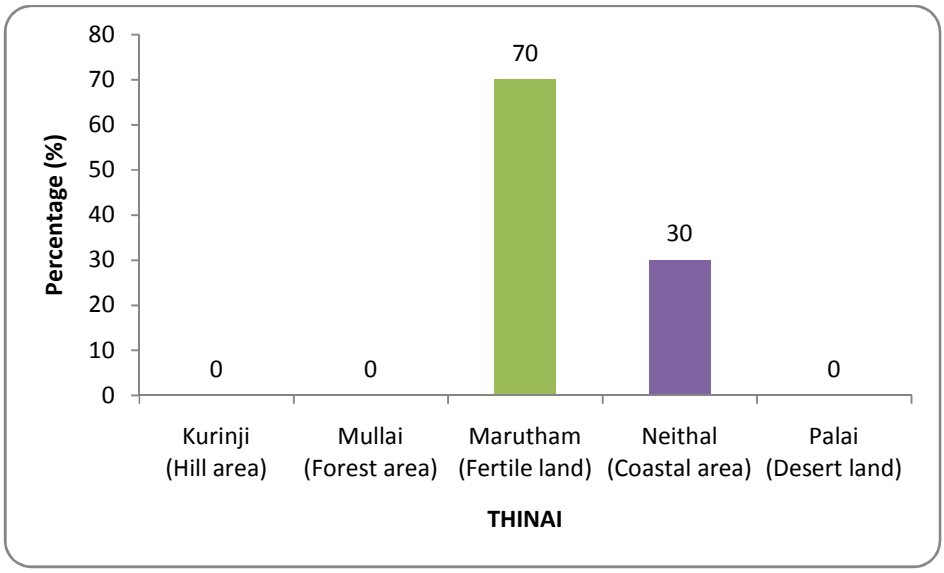
Inference

Among the 50% cases were admitted to the trial in munpanikaalam 25% cases in pinpanikaalam 25% cases in koothirkaalam 17.5% cases in Ilavenirkaalam and remaining 5% cases in kaarkaalam.

6. NILAM

Table 6

S.No	Nilam	No of Cases	Percentage
1	Kurinji	0	0
2.	Mullai	0	0
3.	Marutham	28	70
4.	Neithal	12	30
5.	Palai	0	0
	Total	40	100



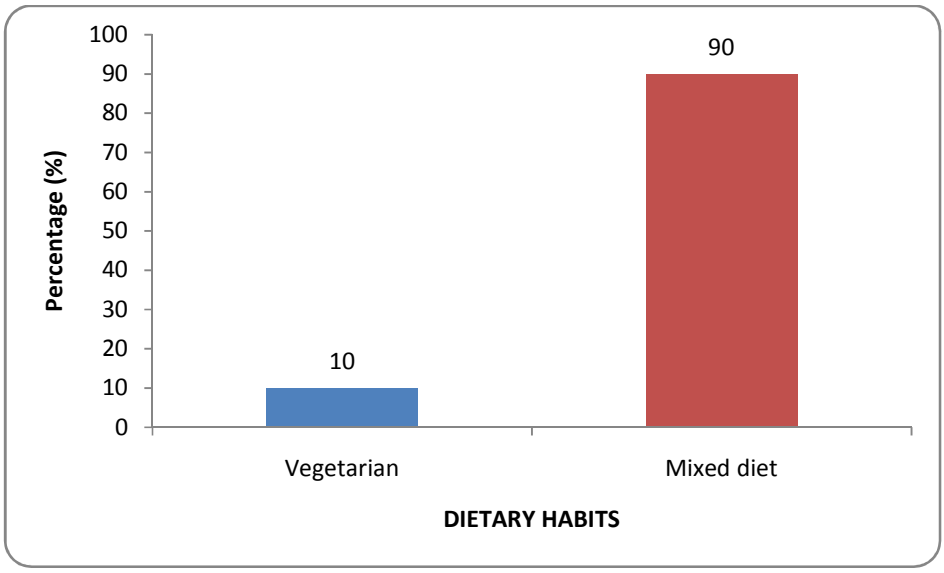
Inference

Among the 40 cases 70% cases were from marutham nilam and the remaining 30% were from Neithal nilam.

7. DIET

Table 7

S.No	Diet	No of Cases	Percentage (%)
1	Vegeratian	4	10
2.	Non vegetarian	36	90
	Total	40	100



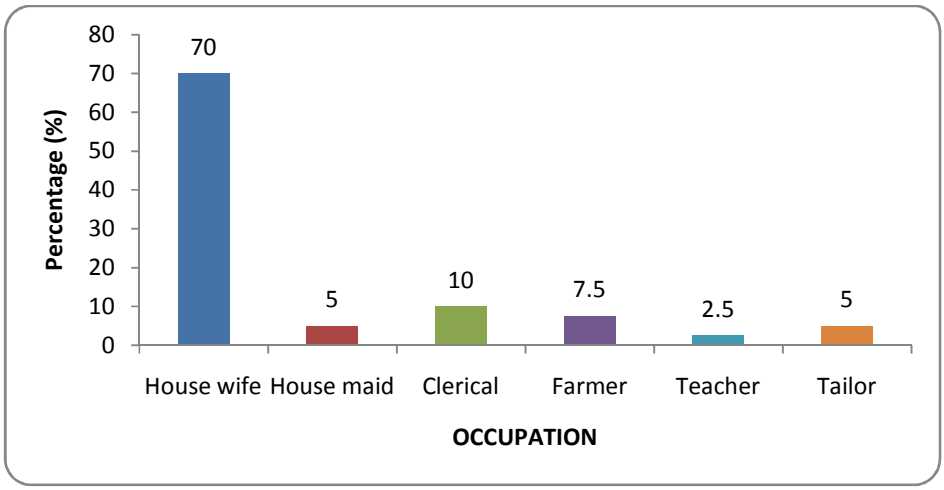
Inference

Among the cases 90% of cases were non vegetarian and 10% of cases were vegetarian.

8. OCCUPATIONAL DISTRIBUTION

Table :8

S.No	Occupation	No of Cases	Percentage (%)
1	House wife	28	70
2.	House maid	2	5
3	Clerical	4	10
4.	Farmer	3	7.5
5.	Teacher	1	2.5
6.	Tailor	2	5
	Total	40	100



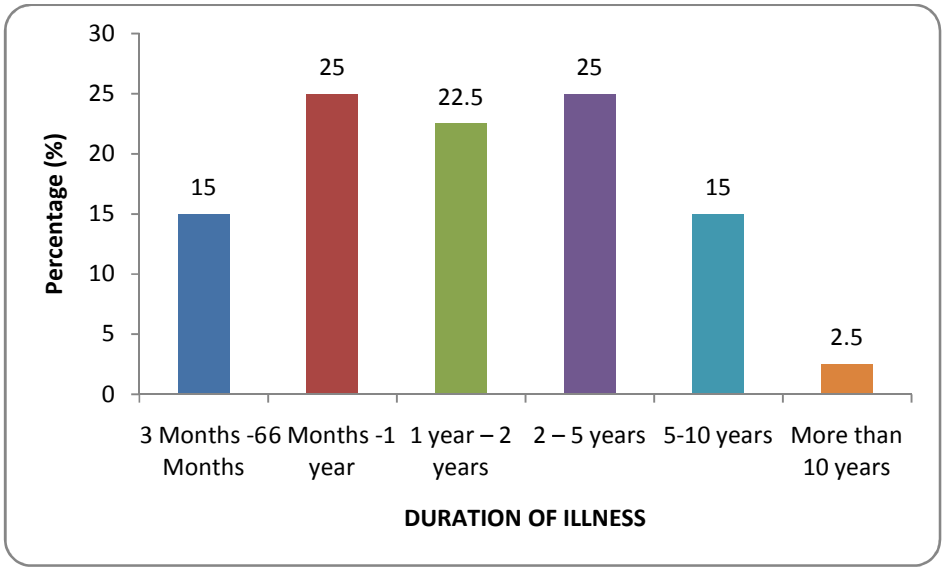
Inference

Among the 40 cases 70% cases were housewife, 5% cases were housemaid, 5% cases were tailor, 2.5% cases were teacher, 10% cases were clerical.

9. DURATION OF ILLNESS

Table : 9

S.No	Duration of illness	No of Cases	Percentage (%)
1	3 Months -6 Months	5	15
2.	6 Months -1 year	10	25
3	1 year – 2 years	9	22.5
4.	2 – 5 years	10	25
5.	5-10 years	5	15
6.	More than 10 years	1	2.5
	Total	40	100



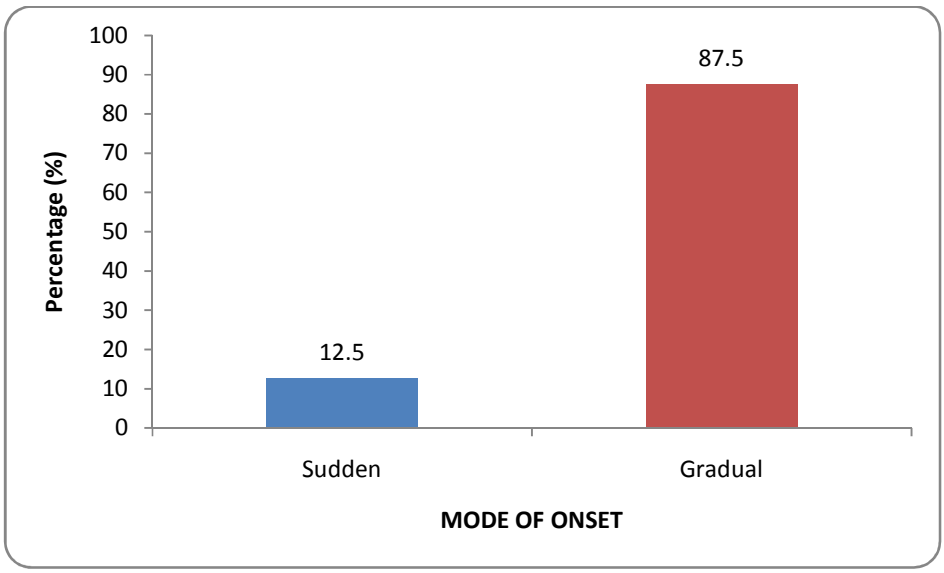
Inference

Among the 40 cases the duration of the illness at the time of study 25% were 6 month – 1 year, 25% were in 2-5 years, 15% were in 5-10 years, 2.5% were in morethan 10 years.

10. ONSET OF THE DISEASE

Table 10

S.No	Mode of onset	No of Cases	Percentage (%)
1	Sudden	5	12.5
2.	Gradual	35	87.5
	Total	40	100



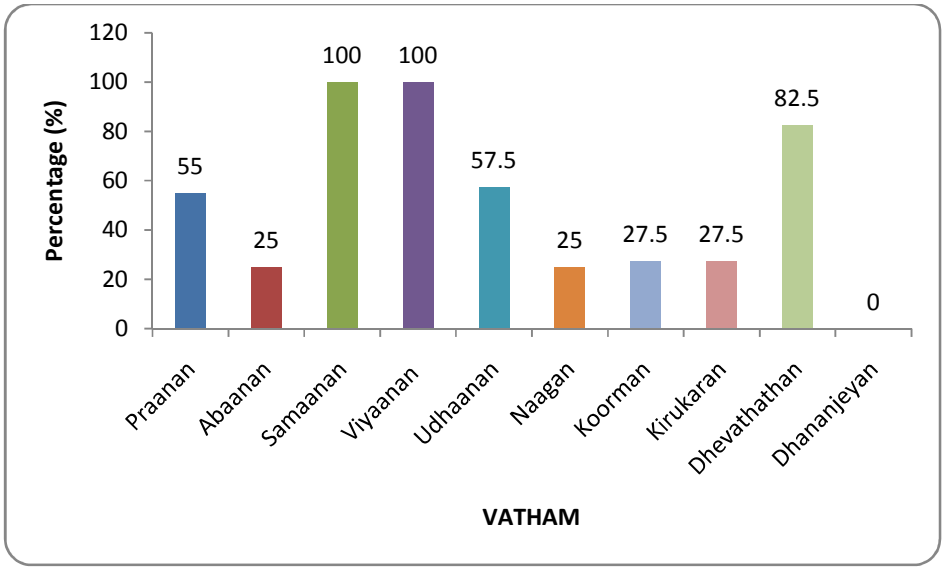
Inference

According to the study 87.5% of cases had gradual onset and 12.5% had sudden onset.

10.A. DISTURBANCES IN VATHAM

Table: 11

S.No	Vatham	Number of cases	Percentage
1.	Praanan	22	55
2.	Abaanan	10	25
3.	Samaanan	40	100
4.	Viyaanan	40	100
5.	Udhaanan	23	57.5
6.	Naagan	10	25
7.	Koorman	11	27.5
8.	Kirukaran	11	27.5
9.	Dhevathathan	33	82.5
10.	Dhananjeyan	0	0



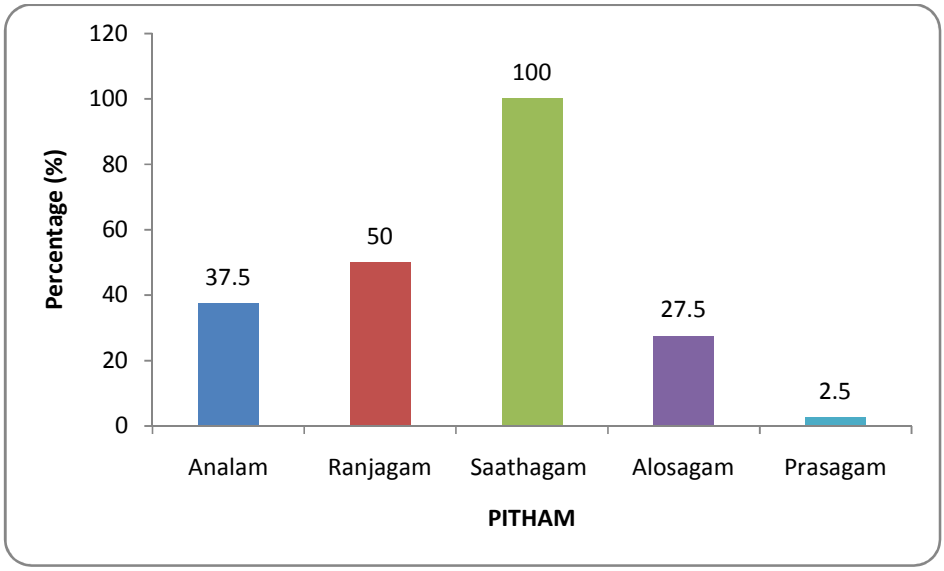
Inference

Among the 40 cases Samanan and viyanan was affected in 100%, Devathathan was affected in 82.5% cases, Udhanan was affected in 57.5% cases, Pranan was affected in 55% of cases koorman and kirukaran was affected in 27.5% cases, abanan was affected 25% cases.

10.B. DISTURBANCES IN PITHAM

Table: 12

S.no	Pitham	Number of cases	Percentage
1.	Analam	15	37.5
2.	Ranjagam	20	50
3.	Saathagam	40	100
4.	Alosagam	11	27.5
5.	Prasagam	1	2.5



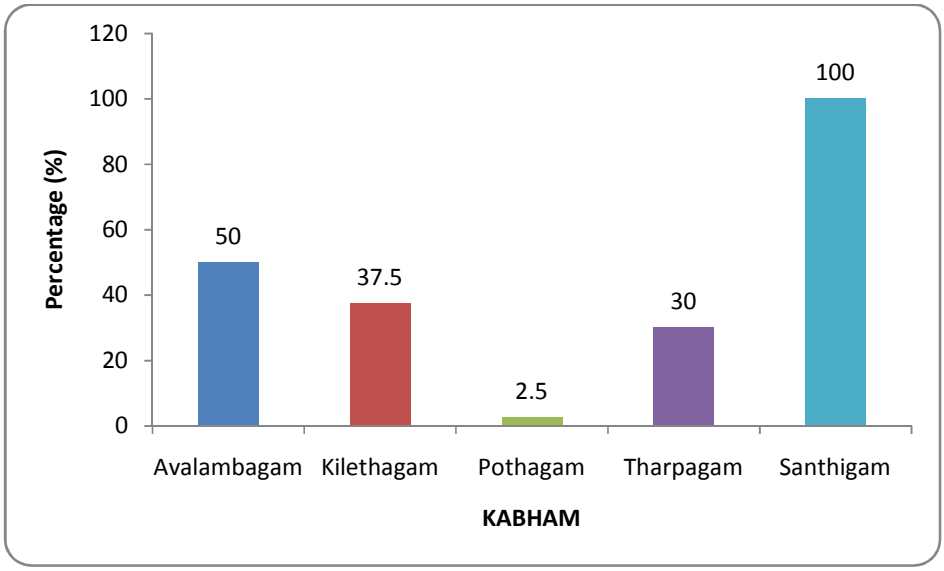
Inference

Among the 40 cases 100% Saathagam affected, 50% ranjagam affected, 37.5% analam affected, 27.5% alosagam affected.

10.C. DISTURBANCES IN KABHAM

Table 13.

S.No	Kabham	Number of cases	Percentage
1.	Avalambagam	20	50
2.	Kilethagam	15	37.5
3.	Pothagam	1	2.5
4.	Tharpagam	12	30
5.	Santhigam	40	100



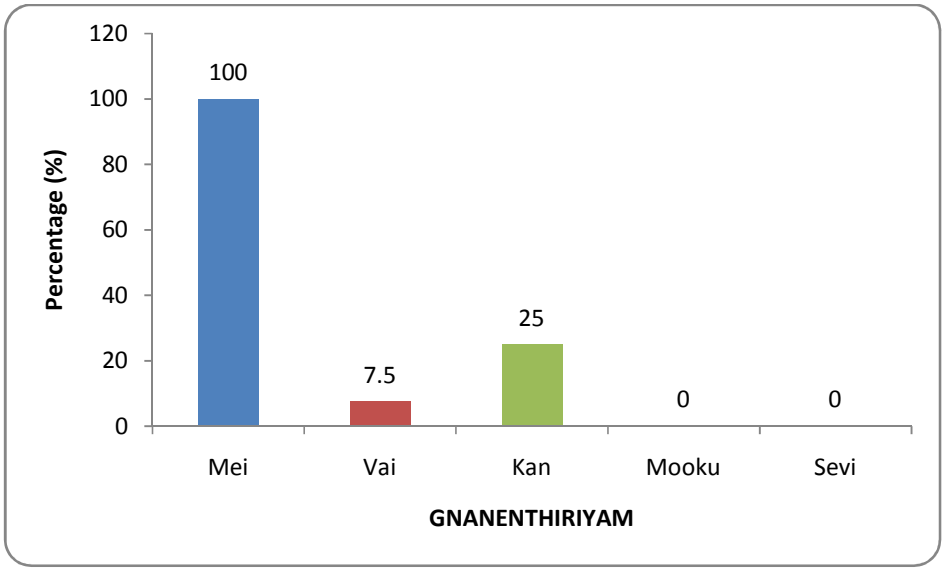
Inference

Among the 40 cases 100% santhigam affected, 30% tharpagam affected, 2.5% pothagam affected, 37.5 kilethagam affected, 50% avalambagam affected.

11. DISTURBANCES IN GNANENTHIRIYAM

Table 14

S.No.	Gnanenthiriyam	Number of cases	Percentage (%)
1.	Mei	40	100
2.	Vai	4	7.5
3.	Kan	12	25
4.	Mooku	0	0
5.	Sevi	0	0



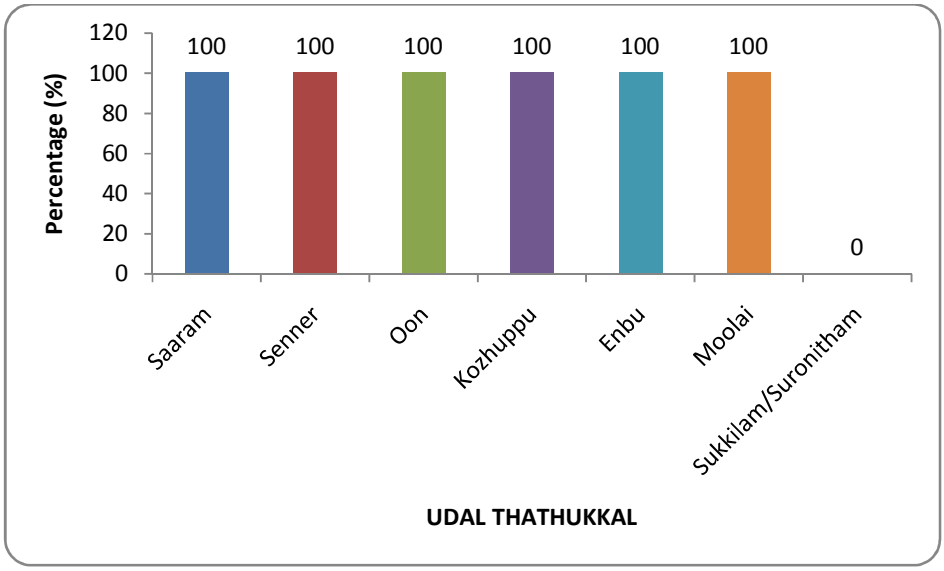
Inference

Among the 40 cases, 100% mei is affected, 7.5% vai is affected, 25% kan is affected.

12. UDAL THATHUKKAL

Table: 15

S.No	Udal thathukkal	NUMBER OF CASES	PERCENTAGE
1.	Saaram	40	100
2.	Senner	40	100
3.	Oon	40	100
4.	Kozhuppu	40	100
5.	Enbu	40	100
6.	Moolai	0	100
7.	Sukkilam/Suronitham	0	0



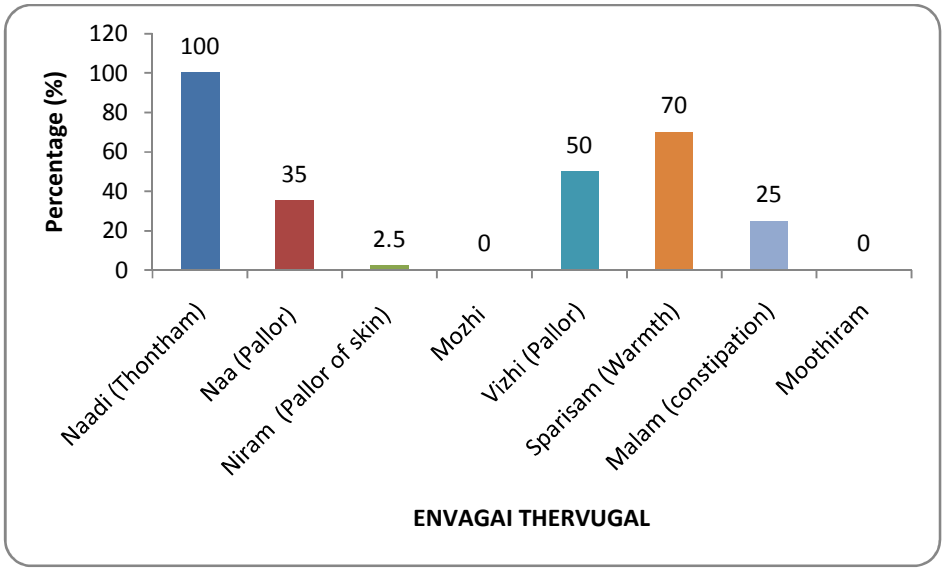
Inference

Among the 40 cases All Udal thathukkal were affected in 100% .

13. ENVAGAITHERVUGAL

Table : 16

S.No.	Envagai thervugal	Number of cases	Percentage
1.	Naadi (Thontham)	40	100
2.	Naa (Pallor)	14	35
3.	Niram (Pallor of skin)	1	2.5
4.	Mozhi	0	0
5.	Vizhi (Pallor)	20	50
6.	Sparisam (Warmth)	28	70
7.	Malam (constipation)	10	25
8.	Moothiram	0	0



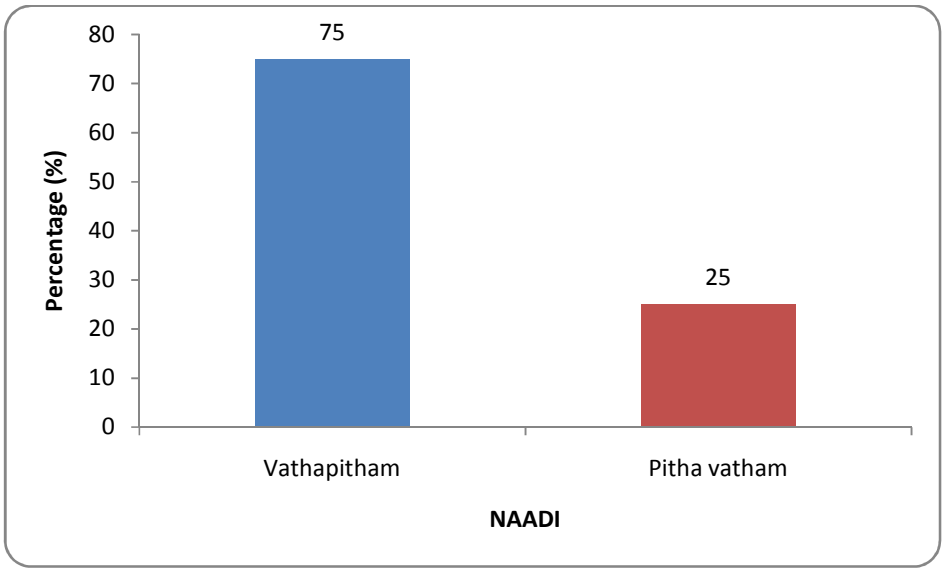
Observation

In all the cases examination of Naadi, Naadi revealed thontham of vatham. Sparisam was affected in 70% cases due warmth felt in the affected joints. Vizhi was affected in 50% cases Naa was affected in 35% cases and malam was affected in 25% cases, Niram was affected in 2.5% cases.

A. **NAADI**

Table 17

S.No.	Parameters	Number of cases	Percentage
1.	Vathapitham	30	75
2.	Pitha vatham	10	25
	Total	40	100



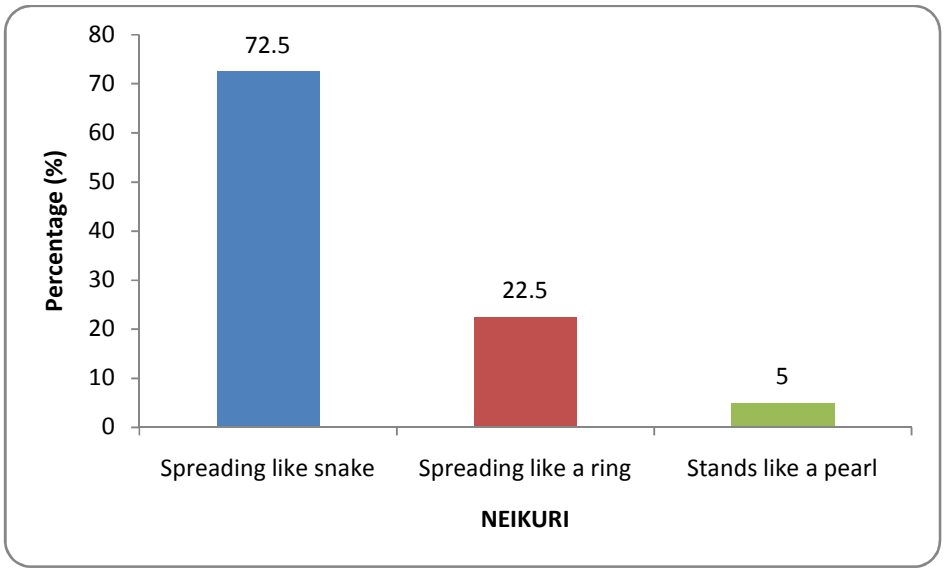
Observation

Among the 40 cases 75% of the cases revealed vatha pitha naadi, 25% of the cases revealed pitha vatham

B. NEIKURI

Table 18: Neikuri Analysis

S.No.	Inference	Number of cases	Percentage (%)
1.	Spreading like snake	29	72.5
2.	Spreading like a ring	9	22.5
3.	Stands like a pearl	2	5



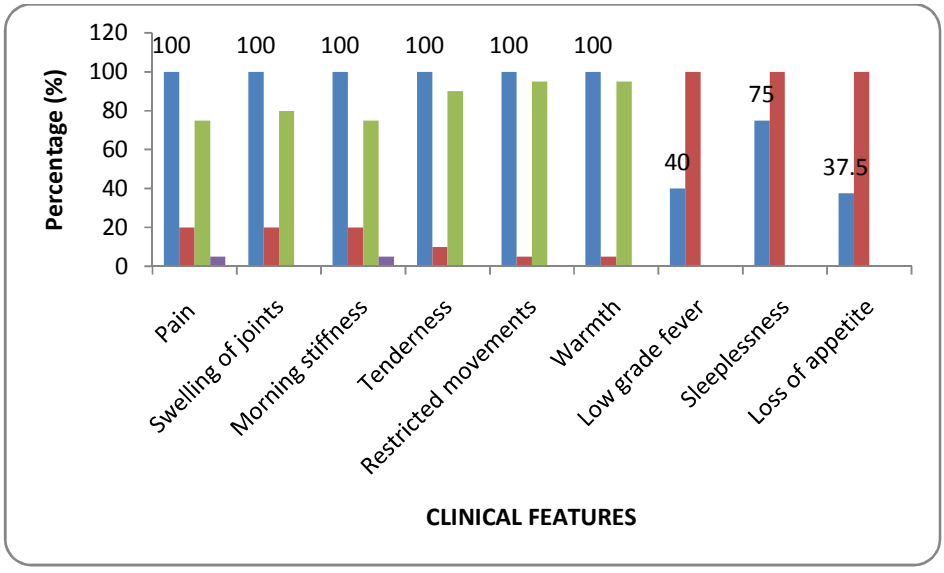
Inference

Among the 40 cases 72.5% was spreading like snake, 22.5% was spreading like a ring, 5% was stands like a pearl.

14. CLINICAL SYMPTOMS (BEFORE AND AFTER TREATMENT)

Table 19

S. No	Clinical features	Before treatment		After treatment					
		No. of cases 40	%	Releived	%	Reduced	%	No improvement	%
1.	Pain	40	100	8	20	30	75	2	5
2.	Swelling of joints	40	100	8	20	32	80	0	0
3.	Morning stiffness	40	100	8	20	30	75	2	5
4.	Tenderness	40	100	4	10	36	90	0	0
5.	Restricted movements	40	100	2	5	38	95	0	0
6.	Warmth	40	100	2	5	38	95	0	0
7.	Low grade fever	15	40	15	100	0	0	0	0
8.	Sleeplessness	30	75	30	100	0	0	0	0
9.	Loss of appetite	15	37.5	15	100	0	0	0	0



Inference Pain, swelling of joints, morning stiffness, tenderness, restricted movement and warmth were found in all the 40 patients before treatment.

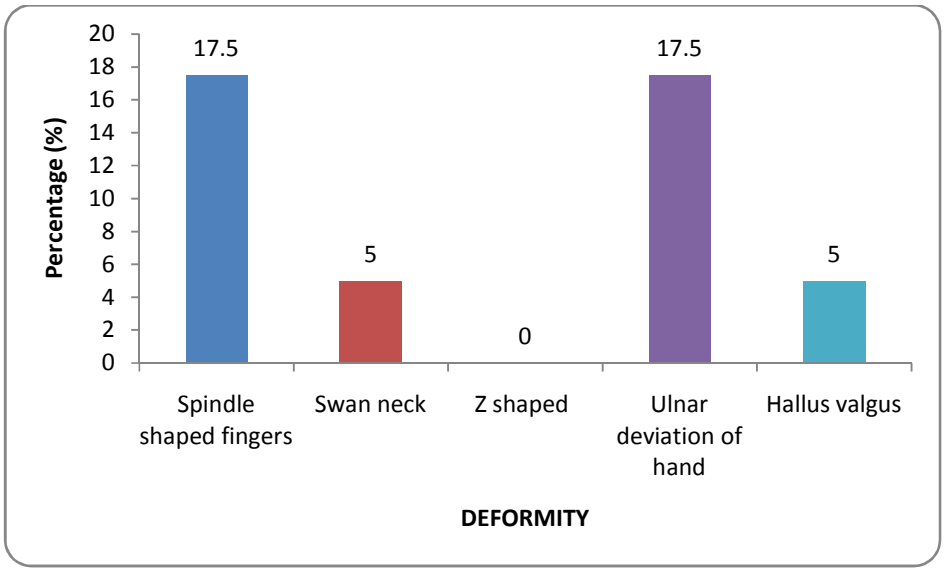
After treatment there was a considerable reduction in all symptoms particularly in pain, morning stiffness, swelling of joints, tenderness, restricted movements and warmth.

After treatment there was a complete relief in the symptoms like low grade fever, sleeplessness and loss of appetite.

15. DEFORMITIES

Table:20

S.No.	Deformity	Number of cases	Percentage
1.	Spindle shaped fingers	7	17.5
2.	Swan neck	2	5
3.	Z shaped	0	0
4.	Ulnar deviation of hand	7	17.5
5.	Hallus valgus	2	5



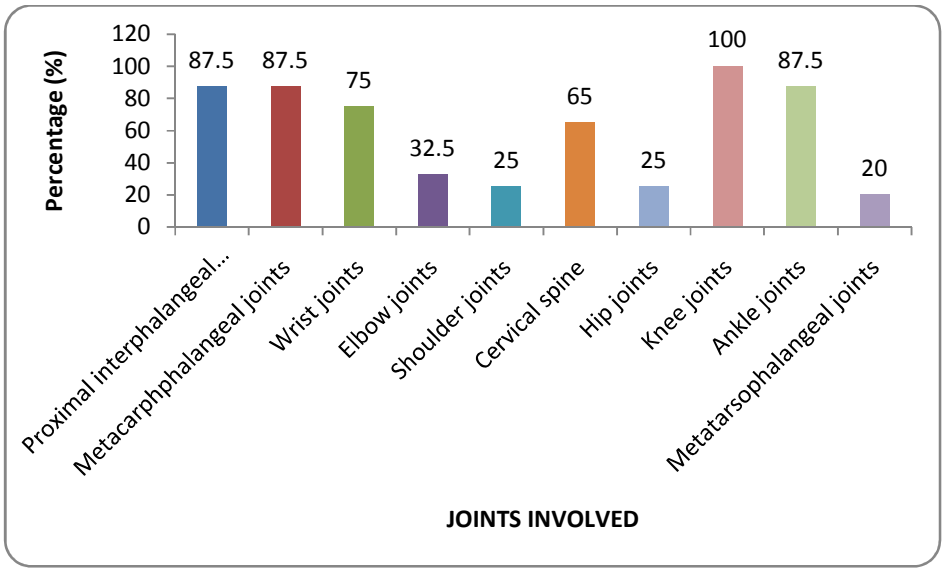
Observation

Among the 40 patients, 17. 5% cases hand spindle shaped fingers, 17.5% cases had ulnar deviation of hand, 5% cases had hallus valgus and 5% cases had swan neck deformity.

16. INVOLVEMENT OF JOINTS

Table :21

S.No.	Joints involved	Number of cases	Percentage
1.	Proximal interphalangeal joints of hand	35	87.5
2.	Metacarphphalangeal joints	35	87.5
3.	Wrist joints	30	75
4.	Elbow joints	13	32.5
5.	Shoulder joints	10	25
6.	Cervical spine	26	65
7.	Hip joints	10	25
8.	Knee joints	40	100
9.	Ankle joints	35	87.5
10.	Metatarsophalangeal joints	8	20

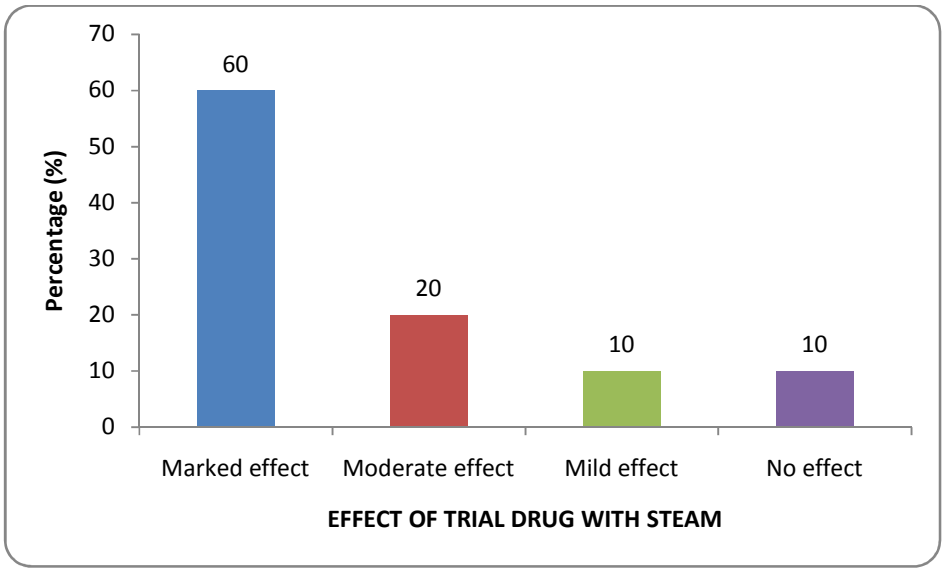


Among the 40 cases 100% had knee joints, 87.5% of the cases had proximal interphalangeal joint, ankle joints and 20% metacarpophalangeal joints, 75% had wrist joints, 65% had cervical spine, 32.5% had elbows, 25% had hip joints, shoulder joints and 20% had meta tarsophalangeal joints

EFFECT OF TRIAL DRUG ALONG WITH COMPLEMENTARY THERAPY

Table - 22

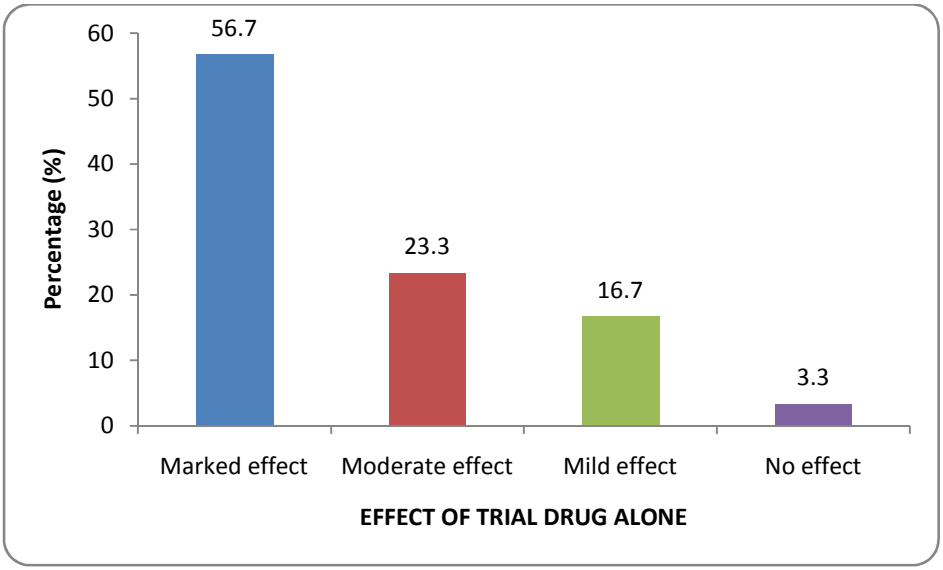
S.No.	EFFECT OF TRIAL DRUG WITH STEAM	Number of cases	Percentage
1.	Marked effect	6	60
2.	Moderate effect	2	20
3.	Mild effect	1	10
4.	No effect	1	10



EFFECT OF TRIAL DRUG ALONE

Table - 23

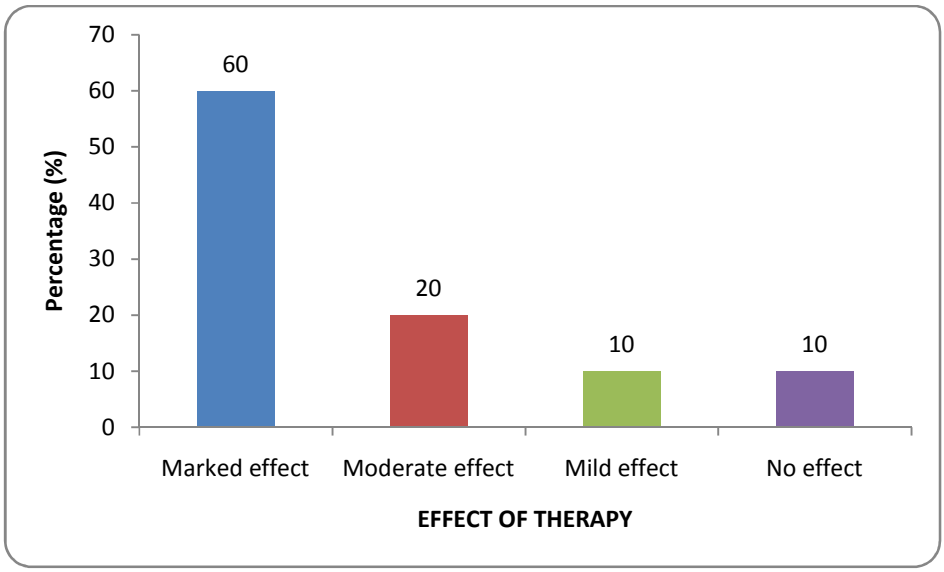
S.No.	EFFECT OF TRIAL DRUG ALONE	Number of cases	Percentage
1.	Marked effect	17	56.7
2.	Moderate effect	7	23.3
3.	Mild effect	5	16.7
4.	No effect	1	3.3



COMPARISION BETWEEN THE EFFECT OF TRIAL DRUG AND TRIAL DRUG ALONG WITH COMPLIMENTARY THERAPY

Table - 24

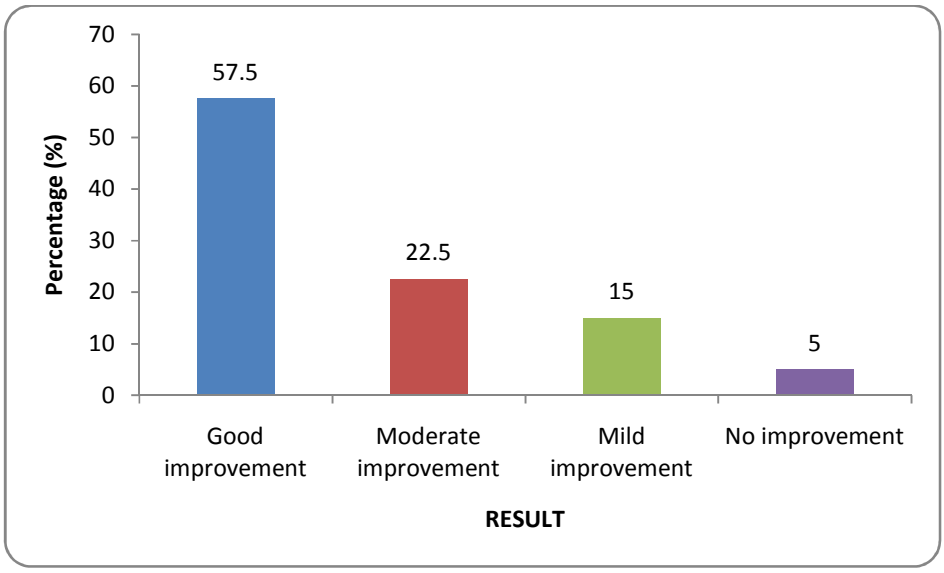
S.No.	EFFECT OF THERAPY	Trial drug alone (%)	Trial drug with steam
1.	Marked effect	56.7	60
2.	Moderate effect	23.3	20
3.	Mild effect	16.7	10
4.	No effect	3.3	10



18. OVERALL REUSLT AFTER TREATMENT

Table : 25

S.No.	Result	Number of cases	Percentage
1.	Good improvement	23	57.5
2.	Moderate improvement	9	22.5
3.	Mild improvement	6	15
4.	No improvement	2	5



Observation

Out of the 40 patients 57.5% of the patients had good improvement, 22.5% had moderate improvement, 15% had mild improvement and 5% had no improvement

Table: 25.(a) List of Out Patients of PG-III Sirappu Maruthuvam Department Given 1. Mathiyoosna rasayanam- Internal 2. Nympathi thylam - External

S.NO	OP.NO	NAME	AGE/SEX	Date of Registration on	Date of Discharge	Total No.of days treated	Symptoms				RESULTS
							P	S	MS	MR	
1	73823	lakshmi	48/F	28.8.17	28.10.17	60	+	+	+	+	Good
2	13009	perratchi	63/F	21.12.17	13.2.18	53	+	+	+	+	Moderate
3	620	Meeral	45/F	2.1.18	16.2.18	44	+	+	+	+	Moderate
4	1558	Kanagavathi	60/F	4.1.18	16.2.18	42	+	+	+	+	Fair
5	1174	Kanagalakshmi	40/F	4.1.18	18.2.18	45	+	+	+	+	Good
6	3330	Sahulhameed	36/M	8.1.18	28.2.18	52	+	+	+	+	Good
7	3545	Revathi	50/F	9.1.18	23.8.18	45	+	+	+	+	Good
8	6228	Rani	45/F	18.1.18	28.2.18	42	+	+	+	+	Moderate
9	9768	Lakshmanan	42/M	30.1.18	16.3.18	46	+	+	+	+	Mild
10	8994	Shanthi	40/F	2.2.18	20.3.18	47	+	+	+	+	Moderate
11	10367	mumtaj	30/F	30.1.18	30.3.18	60	+	+	+	+	Good
12	12563	Mukkammal	52/F	6.2.18	22.3.18	45	+	+	+	+	Moderate
13	13534	Pushapavalli	29/F	8.2.18	22.3.18	42	+	+	+	+	Moderate
14	15850	Rajammal	57/F	8.2.18	24.3.18	45	+	+	+	+	Good
15	17570	Pechimuthu	54/M	20.2.18	10.4.18	49	+	+	+	+	Good
16	18323	Syed ibrahamin	45/M	22.2.18	12.4.18	49	+	+	+	+	Mild
17	22359	Mohideen	43/M	6.3.18	20.4.18	45	+	+	+	+	Moderate
18	22335	Faritha	45/F	6.3.18	24.4.18	49	+	+	+	+	Good
19	22173	Pitchaimari	29/F	7.3.18	5.5.18	61	+	+	+	+	Moderate
20	40846	Raihana	60/F	8.3.18	5.5.18	61	+	+	+	+	Moderte

P- Pain, S – Swelling, MS – Morning stiffness, MR – Movement Restricted

Table 25 (b) Investigation for OP Patients

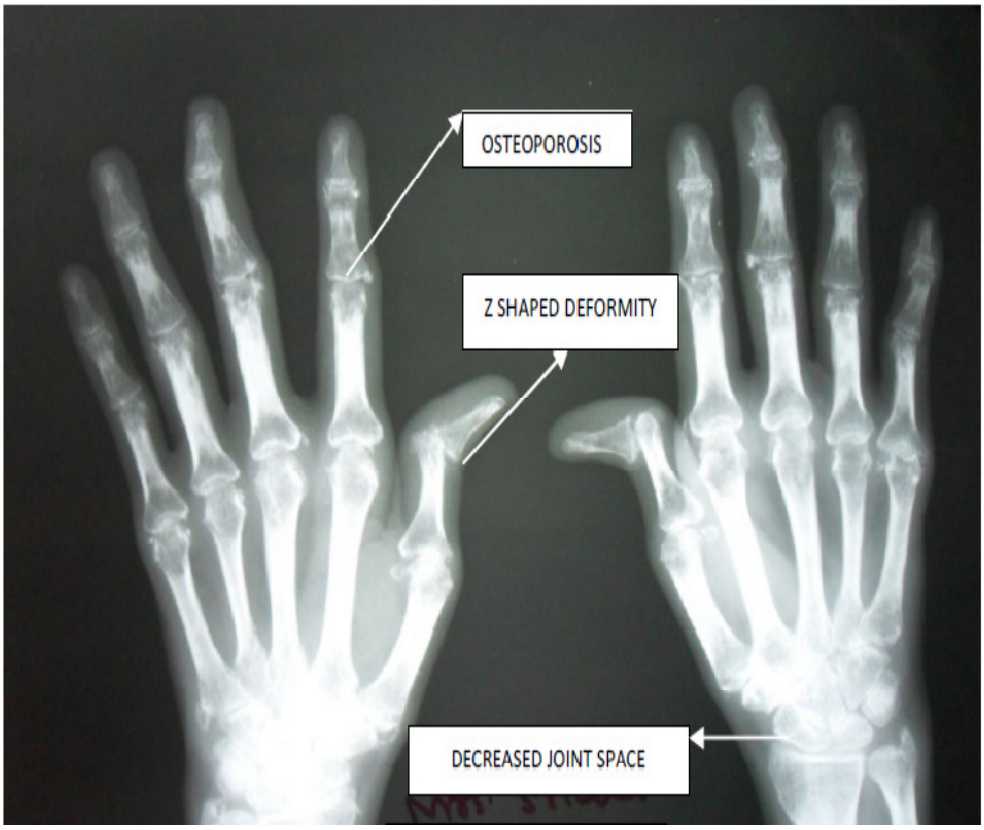
S.No	IP.No	Haemotological Investigation																					Urine Analysis						
		WBC Total		WBC Differential Count (%)						E.S.R. mm/hr				HB (gms%)		BT mgs%			AT mgs%			RA FACTOR		BT			AT		
				BT			AT			BT		AT																	
		BT	AT	P	L	E	P	L	E	1/2 hr	1 hr	1/2 hr	1 hr	BT	AT	BS	BU	BC	BS	BU	BC	BT	AT	Alb	Sug	Dep	Alb	Sug	Dep
1	73823	6000	6200	64	34	2	66	32	2	15	30	15	28	11	12	80	31	102	90	23	106	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
2	13009	8200	8600	72	24	4	72	26	2	27	45	20	42	10.5	11	90	19	162	90	19	158	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
3	620	9500	9400	62	34	4	63	34	3	26	40	25	38	9.8	10.5	80	28	199	80	22	195	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
4	1558	8000	8100	61	33	6	61	34	5	13	44	12	42	9	10.5	109	20	141	105	17	150	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
5	1174	10000	9900	65	34	1	67	33	-	18	40	22	58	9.9	10.5	90	25	126	90	19	120	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
6	3330	8100	8300	73	20	7	74	22	4	80	120	65	90	9.9	11	88	17	198	92	16	194	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
7	3545	11000	11000	50	36	4	60	37	3	20	44	16	38	11.2	11.4	100	12	121	96	15	121	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
8	6228	8800	8400	66	29	5	65	30	5	25	41	24	35	10.4	11.5	108	28	132	108	27	133	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
9	9768	8700	8700	76	23	1	76	23	1	28	45	18	40	8.9	10.6	90	13	137	92	14	135	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
10	8994	7000	7200	68	30	2	67	30	3	45	76	42	72	9.3	10.4	106	21	144	102	19	145	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
11	10367	7500	7800	70	30	-	66	33	1	10	20	6	14	11.5	11.5	112	19	168	110	17	162	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
12	12563	9500	9600	62	36	2	63	34	3	8	10	10	20	12	12.5	80	26	164	82	24	156	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
13	13534	7000	7100	69	28	3	72	27	1	20	38	18	38	11	11.4	82	18	130	90	20	128	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
14	15854	9000	9200	65	30	5	64	31	5	30	54	28	48	11.5	12	109	16	150	107	17	157	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
15	17570	7800	8000	70	26	4	72	25	3	20	60	18	55	9.9	11	96	26	152	88	18	145	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
16	18323	8600	8400	73	25	2	70	24	6	33	40	31	38	11	11.5	110	20	160	109	22	140	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
17	22359	7000	7200	65	32	3	68	28	4	22	41	20	40	12	13	86	28	152	90	25	138	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
18	22335	8100	8200	70	26	4	68	26	6	30	60	26	59	12.5	13	94	24	152	100	22	150	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
19	22173	9100	9000	63	35	2	70	30	-	17	40	13	35	11.8	12.2	101	21	160	105	22	160	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
20	40846	8900	8800	63	30	7	62	36	2	18	42	16	36	10.8	11.5	100	14	187	95	20	160	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD

Table: 26 (a) List of IN Patients of PG-III Sirappu Maruthuvam Department Given 1. Mathiyoosna rasayanam- Internal 2. Nympathi thylam - External

S.NO	IP.NO	NAME	AGE/SEX	D.O.A	D.O.D	NO.OF. DAYS	SYMPTOMS				RESULT
							P	S	MS	MR	
1	963	Mohaideen	58/M	10.4.18	25.5.18	46	+	+	+	+	G00D
2	1023	Muthlakshmi	55/F	16.4.18	25.5.18	40	+	+	+	+	MODERATE
3	821	Jesima	43/F	26.3.18	10.5.18	45	+	+	+	+	MODERATE
4	770	Ponuthai	52/F	20.3.18	30.4.18	40	+	+	+	+	GOOD
5	26	Nagurmeeral	52/F	26.12.17	28.1.18	40	+	+	+	+	GOOD
6	89	Papa	59/F	17.1.18	1.3.18	43	+	+	+	+	MILD
7	94	Airathaal	48/F	18.1.18	28.1.18	41	+	+	+	+	GOOD
8	804	Madaswamy	41/M	22.3.18	22.4.18	31	+	+	+	+	GOOD
9	771	Uthaiyakumar	27/M	20.3.18	25.4.18	36	+	+	+	+	MODERATE
10	1072	Koppammal	54/F	19.4.18	25.5.18	36	+	+	+	+	FAIR
11	99	Rani	45/F	7.4.18	6.6.18	62	+	+	+	+	MILD
12	101	Kumarai	39/F	6.1.18	2.2.18	27	+	+	+	+	MODERATE
13	809	Shanthi	41/F	10.1.18	20.2.18	41	+	+	+	+	MODERATE
14	2783	Kathir	33/M	26.7.17	30.8.17	34	+	+	+	+	MODERATE
15	1053	Mariammal	45/F	7.3.18	20.4.18	43	+	+	+	+	GOOD
16	8994	Bhagavathi	48/F	1.9.17	1.11.18	61	+	+	+	+	GOOD
17	2424	Tamilarasi	45/F	20.4.18	20.5.18	30	+	+	+	+	MILD
18	2630	Vani	45/F	28.4.18	1.6.18	34	+	+	+	+	MILD
19	26798	Rahamed	60/F	1.5.18	30.5.18	29	+	+	+	+	GOOD
20	38219	Murugaesan	40/M	1.5.18	6.6.18	36	+	+	+	+	GOOD

Table 26 (b) Investigation for IP Patients

S.No	IP.No	Haemotological Investigation																					Urine Analysis						
		WBC Total		WBC Differential Count (%)						E.S.R. mm/hr				HB (gms%)		BT mgs%			AT mgs%			RA FACTOR		BT			AT		
				BT			AT			BT		AT																	
		BT	AT	P	L	E	P	L	E	1/2 hr	1 hr	1/2 hr	1 hr	BT	AT	BS	BU	BC	BS	BU	BC	BT	AT	Alb	Sug	Dep	Alb	Sug	Dep
1	963	6200	6200	64	32	4	66	32	2	15	30	15	28	11	12	80	31	108	90	24	106	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
2	101	8200	8600	72	24	4	72	26	2	27	45	20	42	10.5	11	90	19	13	100	20	158	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
3	1023	9500	9000	66	34	0	63	37	0	26	40	25	38	9.8	10.5	80	28	199	80	22	195	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
4	26798	8000	8100	61	33	6	61	35	4	13	44	12	42	9	10.5	109	20	141	105	17	150	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
5	1030	10000	9900	65	34	1	67	33	-	18	40	22	58	9.9	10.5	90	25	126	90	19	120	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
6	809	8100	8200	73	20	7	74	22	4	80	120	65	90	9.9	11	88	17	198	92	16	194	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
7	770	11000	11000	50	36	4	60	37	3	20	44	14	36	11.2	11.4	100	12	121	98	15	121	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
8	2783	8800	8400	66	29	5	65	30	5	25	41	24	35	10.4	11.5	108	28	140	118	27	133	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
9	1072	8700	9000	75	24	1	77	24	1	28	40	18	38	8.9	10.6	90	13	137	92	14	135	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
10	1053	7000	7200	68	30	2	67	30	3	45	76	42	72	9.3	10.4	106	21	144	102	19	145	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
11	771	7500	7800	70	30	-	66	33	1	10	20	6	14	11.5	11.5	112	19	168	110	17	162	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
12	8994	9500	9600	62	36	2	63	34	3	8	10	10	20	12	12.5	80	26	164	82	24	156	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
13	804	7000	7100	69	28	3	72	27	1	20	38	18	38	11	11.4	82	18	130	90	20	128	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
14	2630	9000	9200	65	30	5	64	31	5	30	54	28	48	11.5	12	109	16	150	107	17	157	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
15	26	7800	8000	70	26	4	72	25	3	20	60	18	55	9.9	11	96	26	152	88	18	145	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
16	26798	8600	8400	73	25	2	70	24	6	33	40	31	38	11	11.5	110	20	160	109	22	140	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
17	89	7000	7200	65	32	3	68	28	4	22	41	20	40	12	13	86	28	152	90	25	138	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
18	38219	8100	8200	70	26	4	68	26	6	30	60	26	59	12.5	13	94	24	152	100	22	150	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
19	821	9100	9200	64	34	2	70	30	-	15	38	13	35	11.8	12.2	101	21	160	105	22	146	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD
20	94	8900	8800	63	30	7	62	36	2	18	42	16	34	10	11	101	16	188	96	26	168	+	+	Nil	Nil	1-2 PC	Nil	Nil	NAD


OSTEOPOROSIS
Z SHAPED DEFORMITY
DECREASED JOINT SPACE

DISCUSSION

The main aim of the treatment was to study the Therapeutic effect of the drug MATHIYOOSHNA RASAYANAM to reduce pain, swelling and restricted joint movements in the disease Uthira Vatha Suronitham. The clinical features of Uthiravatha Suronitham can be correlated to Rheumatoid Arthritis in modern science. Rheumatoid Arthritis is a chronic inflammatory, destructive, and deforming symmetrical poly arthritis associated with symmetrical involvement of joints.

Uthiravatha Suronitham is a Vatha disease in which, there occur a derangement of Vatha thathu and Pitha thathu.

Among the 40 patients selected

According to the **Age group** 41-50 was42..5%, 31-40was 12.5 and 51-60 were 30%, 61-70 was 2.5%, 21-30 was 10.

In **Gender** among the 40 patients seleced, the disease (R.A) was found to be higher in females (97.5%) and lower in males (2.5%)

In **Religion** among the 40 cases observed, 75% of the cases were hindu, 20% of the cases were muslim and 2% of the cases were christians.

In **Body constitution** out of 40 cases all the 100% cases were came under thontha thegi.

In **Paruvakaalam** (season) out of 40 cases, 35% cases were included in munpani kaalam, 30% cases were in pinpanilkaalam, 15% cases were in koothir kaalam, 12.5% cases were in Ilavenil kalam and 7.5% cases in kaar kalam.

In **nilam** out of 40 cases, 70% cases were from marutha nilam and the remaining 30cases were neithal nilam30.%vegetarian diet.

In **occupational distribution** out of 40 cases, 62.5% were house wives, 12.5% were farmer, 10% were house maids, 7.5% were tailors, 5% were teachers, and 2.5% were clerical.

In **duration of illness** out of 40 cases 25% were 1 year – 2 years, 22.5% were 3 months – 6 months and 2-5 years, 20% were 6 months – 1 year, 7.5% were 5-10 years, and 2.5% were more than 10 years.

In **onset of symptoms** out of 40 cases, 77.5% of the cases had gradual onset and 22.5% had sudden onset.

In **vatham** out of 40 cases, samaanan vyaanan were affected in 100% cases, Dhevathathan was affected in 82.5% cases, udhanan was affected in 57.5% cases, praanan was affected in 55% cases, koorman, kirukaran were affected in 27.5% cases, naagan was affected in 25% cases, abaanan was affected in 15% cases.

In **pitham** out of 40 cases, saathagam was affected in 100% cases, Analagam was affected in 37.5% cases, Ranjagam was affected in 50% cases, Alosagam was affected in 27.5% cases, Prasagam was affected in 2.5% cases.

In **kabam** out of 40 cases santhigam was affected in 100% cases, avalambagam was affected in 50% cases, kilethagam was affected in 37.5% cases, tharpagam was affected in 30% cases, pothagam was affected in2. 5% cases.

In **gnanenthriyam** out of 40 cases, all 40 (100%) cases had mei affected, 10(25%) cases kan was affected, 3(7.5%) cases vai was affected.

In **kanmenthriyam** out of 40 cases kai and kaal (Upper and lower limbs) are affected in all (100%) of the case, eruvai was affected in 10% of cases, vai was affected in 7.5% of cases.

In **udal thathukkal** out of 40 cases, saaram , senneer , oon , kozhuppu, enbu ,moolai 100% were affected.

In **envagai thervugal** among the 40 cases, sparisam was affected in 70%, vizhi was affected in 50% cases, naa was affected in 35.5% cases, malam was affected in 25% cases niram was affected in 2.5% cases.

While seeing the **Naadi** among the 40 cases vatha pitha naadi was found in 75% cases and pitha vatha naadi was found 25% cases.

In **neikkuri,** among the 40 cases, 77.5% of the cases showed vathaneer, 17.5% of the cases showed kabaneer, 5% of the cases showed pithaneer.

According to the **clinical features** all 100% of cases had pain, swelling of the joints, early morning stiffness, tenderness, restricted movements and warmth, 75% cases had sleeplessness, 40% cases had fever, 37.5% cases had loss of appetite.

According to **deformities** in my study 17.5% cases had spindle shaped fingers, 17.5% cases had ulnar deviation of hand, 5% cases had hallus valgus and1 7.5% cases has swan neck deformity.

Involvement of joints in my study, 100% had knee joints, 87.5% of the cases had proximal interphalangeal joints, ankle joint and metacarpophalangeal joints, 75% had wrist joints, 65% had cervical spine, 32.5% had elbows, 25% had hip joints, shoulder joints and metatarsophalangeal joints.

After treatment out of 40 cases

In my study, before treatment 100% of cases had pain, swelling of joints, morning stiffness, tenderness, restricted movements and warmth. 75% of cases had sleeplessness, 40% of cases had low grade fever and 15% cases had loss of appetite.

After treatment 15% of cases had relieved and 80% of cases had reduced and 5% of cases had no improvement in pain.

Over all **Results** are in my 57.5% cases showed Good improvement, 22.5% cases showed Moderate improvement, 15% cases showed mild improvement 5% cases showed no improvement.

SUMMARY

Yugi Muni classified vatha diseases into 80 types one among them is uthiravatha suronitham.In modern uthiravatha suronitham is compared with Rheumatoid arthritis. It is the most common persistent inflammatory arthritis, occurring throughout the world and in all ethnic groups with intermittent exacerbations.

The aim of the study was to evaluate the efficacy of Mathiyooshna Rasayanam and Nympathy thylam in Uthiravatha Suronitham.

Based on the inclusion and exclusion criteria in the approved protocol 40 cases were diagnosed clinically Out of the 40 cases, 20 cases were admitted and treated with the trial Drugs Mathiyooshna Rasayanam [internal] and Nympathy thylam [external] in the In-patient ward and the rest were treated in Outpatient department of Sirappu Maruthuvam in Government Siddha Medical College, Palayamkottai.

Among the 20 Ip patients, 10 IP patients were treated by Steam bath treatment along with the trial medicine and remaining 30 cases were treated only with the trial drugs for 48 days.

In this study, first the patients were well informed about the study and they were asked to sign the consent form. After signing the consent form, information sheet and diatery advice forms were given to the patients.

The various Siddha methods of examination of the disease were carried out and the data were recorded in the prescribed Proforma for the 40 selected cases.

Purgation was given by administering Moolakudori ennai 15ml is given in early morning to bring the Thirithodam to equilibrium a day prior to treatment and the patient was given complete rest on the day of purgation.

The prognosis of the patients during each visit was entered and monitored for any adverse drug reactions or poor patient compliance, investigation reports were recorded before and after treatment.

Bio-chemical analysis revealed that the drug contains Calcium, Ferrous iron, tannic acid, reducing sugar and Unsaturated compounds.

The pain assessment was done in all the 40 patients participated in the trial using the universal pain assessment scale and at the end of the study the results showed, the mean pain score before treatment was 3.85 and after treatment it was reduced to 2.33

Among the 20 IP patients, 10 IP patients were given Steam bath treatment along with their internal medicine. The remaining 10 IP patients didn't received steam bath treatment. The results are compared at the end of the study. The mean pain score of the 10 patients who received steam bath treatment before treatment is 4.3 and after treatment it is reduced to 1.7. Hence steam bath treatment along with internal medicine is more effective in the treatment of rheumatoid arthritis

From this clinical trial it could be inferred that Mathiyooshna Rasayanam and Nympathy thylam possess good therapeutic efficacy in Uthiravatha suronitham.

Good Improvement	**-**	**23 Patients (57.5%)**
Moderate Improvement	**-**	**9 patients (22.5%)**
Mild Improvement	**-**	**6 patients (15%)**
No improvement	**-**	**2 patients (5%)**

CONCLUSION

The result of this clinical trial indicate that trial drug is clinically effective in Uthira vatha Suronitham. The toxicity study reveals that the trial drug mathiyooshna rasayanam is safe. Mathiyooshna Rasayanam have analgesic and anti inflamatory activity.

The main aim of the treatment was to study the Therapeutic effect of the drug Mathiyooshna Rasayanam by its action on Pain, swelling, morning stiffness, restricted movements etc,.

In this study it was found that about 77.5% of patients were women and after taking internal and external medicine it was found that they felt better and were able to do their day to day work without anyothers help.

Hence the study concludes that, the trial drugs are clinically effective in reducing the pain, swelling and morning stiffness, restricted movements in Uthiravatha suronitham patients. However further work with large number of patients should be carried out towards finding the ideal dose response.

The treatment was aimed at normalizing the deranged thodams and providing relief from symptoms.

There were no adverse reactions complained during the trial.

Because of the encouraging clinical outcome, the study may be further carried out with the same drug in a large number of cases.

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ANNEXURE -I

PREPARATION OF TRIAL DRUG

INGREDIENTS

Internal medicine: MATHIYOOSHNA RASAYANAM

S.No	Ingredient	Botanical name	Part used	Measurement
1	Paranki pattai	*Smilax china*	Root tube	10palam(350 grams)
2	Jathipathri	*Myristica fragrans*	Pericarp	¼palam(8.75grams)
3	Milagu	*Piper nigrum*	Unriped fruit	¼palam(8.75grams)
4	Vaivilangam	*Embelia ribes*	Dried fruits	¼palam(8.75grams)
5	Chukku	*Zingiber officinale*	Dried rhizome	¼palam(8.75grams)
6	Santhanam	*Santalum album*	Wood	¼palam(8.75grams)
7	Kadukkai	*Terminalia chebula*	Pericarp	¼palam(8.75grams)
8	Thippili	*Piper longum*	Fruit	¼palam(8.75grams)
9	Nelli paruppu	*Phyllanthus emblica*	Dried fruit	¼palam(8.75grams)
10	Lavanga pattai	*Cinnamomum verum*	Bark	¼palam(8.75grams)
11	Ealakkai	*Elettaria cardamomum*	Seed	¼palam(8.75grams)
12	Kirambu	*Syzygium aromaticum*	Flower buds	¼palam(8.75grams)
13	Thanri kaai	*Terminalia bellirica*	Dried fruit	¼palam(8.75grams)
14	Sevviyam	*Piper nigram*	Root	¼palam(8.75grams)

15	Jeeragam	*Cuminum cyminum*	Seed	¼palam(8.75grams)
16	Thippili moolam	*Piper longum*	Root	¼palam(8.75grams)
17	Kandu parangi	*Clerodendrum serratum*	Root	¼palam(8.75grams)
18	Vetpalai	*Wrightia tinctoria*	Seed	¼palam(8.75grams)
19	Arathai	*Alpinia galanga*	Rhizome	¼palam(8.75grams)
20	Vaaluluvai arisi	*Clestrus paniculatus*	Seed	¼palam(8.75grams)
21	Korai kilangu	*Cyperus rotundus*	Root tuber	¼palam(8.75grams)
22	Nannari	*Hemidesmus indicus*	Root	¼palam(8.75grams)
23	Kostam	*Costus speciosus*	Rhizome	¼palam(8.75grams)
24	Sadaamaanjil	*Nardostachys grandiflora*	Root	¼palam(8.75grams)
25	Annachipoo	*Illicium verum*	Flower	¼palam(8.75grams)
26	Adhimathuram	*Glycyrrhiza glabra*	Root	¼palam(8.75grams)
27	Kaattu milagu	*Piper nigrum*	Seed	¼palam(8.75grams)
28	Krosani Omam	*Hyoscyamus niger*	Seed	¼palam(8.75grams)
29	Omam	*Carum copticum*	Seed	¼palam(8.75grams)
30	Mullai ver	*Jasminum trichotomum*	Root	¼palam(8.75grams)
31	Honey			325 ml
32	Ghee			Equal to all remaining parts

Purifications of drugs:

- Raw drugs will be heated to a golden brown colour and cooled it.
- In kadukkai seed is removed.
- Paranki pattai should be dried and pulverized. Then should be boiled by steam of milk.

- In chukka outer skin to be removed.
- All roots to be cleaned thoroughly by water and dried in shadow.

Preparation:

Purified dry drug is taken and powdered. Then it is filtered using pure white cloth, honey to be added. Add ghee and make like a Pittu. Keep in airtight container

Method of preparation

The purified dried raw drugs are powdered and shifted well separately

Equal quantity of each powdered drugs are then mixed well. Add honey and ghee and mix well to make it like a pittu.

External medicine: NYMPATHY THAILAM

S. No:	**Ingredient**	**Botanical name**	**Part used**	**Measurement**
1.	Veppennai (Neem oil)	Azadirachta indica	Seed oil	¼ padi (325 ml)
2.	Nallennai (Gingilee oil)	Sesamum indicum	Seed oil	¼ padi (325 ml)
3.	Chadurakalli juice	Euphorpia antiquorum	Extract	½ padi(650 ml)
4.	Maampattai chaaru	Mangifera indica	Pattai	½ padi(650 ml)
5.	Maangolunthu chaaru	Mangifera indica	Leaf	½ padi (650 ml)
6.	Maampoo chaaru	Mangifera indica	Flower	½ padi (650 ml)
7.	Erukkam ver pattai chaaru	Calotropis gigantean	Root	½ padi (650 ml)
8.	Etti kottai	Strychnos nuxvomica	Seed	15

Method of preparation:

Grind the Etti kottai to kalkam , mix the kalkam with all other extracts, and heat until required consistency formed. Filter it then kept in a dry airtight container.

TRIAL DRUG

Internal medicine

- **பறங்கிப்பட்டை**

சுவை

செய்கை

- உடற்தேற்றி
- மேகப்பணி விலக்கி
- காமம் பெருக்கி

குணம்

“தாகம் பலவாகதந் தாது நட்டம் புண் பிளவை

மேகங் கடிகிரந்தி வீழ்மூலந்ஙு தேகமுடன்

குட்டை பகந்த மேற் கொள்வமனம் போம் பறங்கிப்

பட்டையினை யுச்சரித்துப் பார்”

பொருள்

நீர் வேட்கை, முடவாதம், குறே நோய், நீரிழிவு, கடிவிடம், புண் இவை நீங்கும்

Chemical constituents

7-o-seta-D-gluco pyranoside, engeletin, isoengeletin, kaemiferol, rutin, vanillic acid

- **முல்லை வேர்**

பயன்படும் உறுப்பு : வேர்

சுவை - கைப்பு, தன்மை - வெப்பம், பிரிவு - கார்ப்பு

செய்கை

- புழுக்கொல்லி
- வீக்கமுருக்கி
- சிறுநீர் பெருக்கி
- ருதுவுண்டாக்கி

குணம்

முக்கற்றம், தலைநோய், உடல் வெப்பம், கண்படலம் இவை நீங்கும், மனக்கலக்கத்தை போக்கும்.

❖ **சுக்கு**

English Name : Dried Ginger

Botanical Name : Zingiber officinale

Family : Zingiberaceae

Part used : Dried rhizome

Other names in Tamil : அருக்கன், விடமூடிய அமிர்தம், நவசுறு, உலர்ந்த இஞ்சி

Constituents : Zingerd, adenine, shogaol, isovanillin.

Organoleptic characters

Taste : Acrid

Potency : Hot

Division : Acrid

Therapeutic Actions

வெப்பமுண்டாக்கி - Stimulant

பசித்தீத்தூண்டி - Stomachic

அகட்டுவாய்வகற்றி - Carminative

Therapeutic Effect

“வாதப் பிணிவயி றூதற் செவிவாய்
வலிதலை வலிகுலை வலியிரு விழிநீர்
சீதத் தொடுவரி பேதிப் பலரோ
சிகமலி முகமக முகமிடி கபமார்
சீதச் சுரம்விரி பேதச் சுரநோய்
தெறிபடுமெனமொழி குவர்புவி தனிலே
ஈதுக் குதவுமி தீதுக் குதவா
தெனும்விதி யிலைநவ சுறுகுண முனவே”

- தேரையர் குணவாகடம்

❖ **சந்தனம்**

English Name	:	Sandal wood
Botanical Name	:	Santalum album
Family	:	Santalaceae
Part used	:	Wood
Constituents	:	Teresantalol, Santalic acid, Santalone, Santene.

Organoleptic characters

Taste	:	Bitter, astringency
Potency	:	Cold, hot
Division	:	Sweet

Therapeutic Actions

உடற்றேற்றி	-	Alterative
சிறுநீர்ப்பெருக்கி	-	Diuretic
வியர்வைப்பெருக்கி	-	Diaphoretic
வெப்பமுண்டாக்கி	-	Stimulant
அழுகல்மணமகற்றி	-	Disinfectant
துவர்ப்பி	-	Astringent
குளிர்ச்சியுண்டாக்கி	-	Cooling

Therapeutic Effect

"கோதில் சந்தனஞ் சீதோஷ்ணங் கொண்டிருக்கும்

வாதபித்தம் ஐயம் மனப்பிரமை – ஓதுசுரம்

மேகம் தனித்தாகம் வெப்பு சொறி யும்போக்கும்

ஆகந் தனக்குறுதி யாம்"

முக்குற்றம், மனக்கலக்கம், உட்சூடு, ஒழுக்கு வெள்ளை, நாவறட்சி, நமைச்சல் இவை நீங்கும். உடல் வன்மை பெறும்.

❖ **கடுக்காய்**

English Name : Ink nuts, chebulic myrobalan

Botanical Name : Terminalia chebulla

Family : Combretaceae

Part used : Pericarp

Other names in Tamil : அம்மை, மேகம், ஜீவந்தி, அரிதகி, தேவி, வரிக்காய்

Constituents : Ethyl galate, chebulin, corilagin, chebulegic acid.

Organoleptic characters

Taste : Astringency(more); sweet, sour, acrid, bitter (less).

Potency : Hot

Division : Sweet

Therapeutic Actions

வாதமடக்கி - Antivatha

பசித்தீத்தூண்டி - Stomachic

உடற்றேற்றி - Alterative

Therapeutic Effect

"தாடை கழுத்தக்கி தாலு குறியிவிடப்

பீடை சிலிபதமுற் பேதிமுடம் - ஆடையெட்டாத்

தூலமிடி புண்வாத சோணிகா மாலையிரண்

பாலமிடி போமவரிக்கா யால்".

கடுக்காயினால், கன்னம், கழுத்து, நா, ஆண்குறி இவ்விடங்களில் நோய்கள், காலடிப்புற்றுநோய், அதிதூலம், இடிப்புண், வாதசோணிதவாதம், காமாலை, தாவரசங்கம விடங்கள் இவை போம்.

❖ **திப்பிலி**

English Name	:	Long pipper
Botanical Name	:	Piper longum
Family	:	Piperaceae
Part used	:	Fruit
Other names in Tamil	:	ஆதிமருந்து, வைதேகி, அம்பு, குடாரி, சரம்
Constituents	:	Piperin, rutin, piperamine, pinene.

Organoleptic characters

Taste	:	Sweet
Potency	:	Hot
Division	:	Sweet

Therapeutic Actions

வெப்பமுண்டாக்கி	-	Stimulant
அகட்டுவாய்வகற்றி	-	Carminative

Therapeutic Effect

"இருமல் குன்மம் இரைப்பு கயப்பிணி
ஈளை பாண்டு சந்யாசம் அரோசகம்
பொருமல் ஊதை சிரப்பிணி மூர்ச்சைநோய்
பூரிக் குஞ்சல தோடம் பீலிகமும்
வரும லப்பெருக் கோடு மகோதரம்
வாதம் ஆதிமுத் தோடஞ் சுரங்குளிர்
பெருமாலைப்புரி மேகப் பிடகமும்
பேருந் திப்பிலிப் பேரங்குரைக்கவே"

❖ **நெல்லிப்பருப்பு**

English Name : Indian Gooseberry

Botanical Name : Phyllanthus emblica

Family : Euphorbiaceae

Part used : Dried fruit

Other names in Tamil : ஆமலகம், தாத்திரி, கோரங்கம், மிறுதுபலா, ஆம்பல்

Constituents : Emblicanin A & B, glutamic acid, Vitamin C.

Organoleptic characters

Taste : Sour, Acrid, Sweet

Potency : Cold

Division : Sweet

Therapeutic Actions

துவர்ப்பி - Astringent

Therapeutic Effect

"நெல்லிக்காய்க் குப்பித்தம் நீங்கு மதன்புளிப்பால்
செல்லுமே வாதமதிற் சேர்துவரால் - சொல்லுமையம்
ஓடுமிதைச் சித்தத்தில் உன்ன அனலுடனே
கூடுபிற மேகமும் போங் கூறு.

❖ **ஏலக்காய் அரிசி**

English Name	:	Cardamom seeds
Botanical Name	:	Elettaria cardamomum
Family	:	Zingiberaceae
Part used	:	Seed
Other names in Tamil	:	ஆஞ்சி, கோரங்கம், துடி
Constituents	:	Limonene, cineole, terpinolene.

Organoleptic characters

Taste	:	Acrid
Potency	:	Hot
Division	:	Acrid

Therapeutic Actions

வெப்பமுண்டாக்கி	-	Stimulant
அகட்டுவாய்வகற்றி	-	Carminative
பசித்தீத்தூண்டி	-	Stomachic

Therapeutic Effect

"தொண்டை வாய்கவுள் தாலுகு தங்களில்
தோன்றும் நோயதி சாரம்பன் மேகத்தால்
உண்டை போல்எழுங் கட்டி கிரிச்சரம்
உழலை வாந்தி சிலந்தி விஷஞ்சுரம்
பண்டை வெக்கை விதாகநோய் காசமும்
பாழுஞ் சோமப் பிணிவிந்து நட்டமும்
அண்ட யீளைவன் பித்தம் இவைக்கெல்லாம்
ஆல மாங்கமழ் ஏல மருந்ததே..."

❖ **கிராம்பு**

English Name	:	Cloves
Botanical Name	:	Syzygium aromaticum
Family	:	Myrtaceae
Part used	:	Flower buds
Other names in Tamil	:	இலவங்கம், அஞ்சுகம், திரளி, உற்கடம்
Constituents	:	Eugenol. eugenitin, eugenin, Kaempferol.

Organoleptic characters

Taste	:	Acrid
Potency	:	Hot
Division	:	Acrid

Therapeutic Actions

இசிவகற்றி	-	Antispasmodic
அகட்டுவாய்வகற்றி	-	Carminative
பசித்தீத்தூண்டி	-	Stomachic

Therapeutic Effect

"பித்த மயக்கம் பேதியொடு வாந்தியும்போம்
சுத்திவிரத் தக்கடுப்புந் தோன்றுமோ – மெத்த
இலவங்கங் கொண்டவருக் கேற் சுகமாகும்
மலமங்கே கட்டுமென வாழ்த்து."

❖ **கண்டுபரங்கி**

சுவை - கைப்பு, துவர்ப்பு, தன்மை - வெப்பம், பிரிவு - கார்ப்பு

செய்கை

- வெப்பமுண்டாக்கி
- தாது வெப்பகற்றி

குணம்

முக்குற்றம்,இரைப்பிருமல்,உள் வெப்பம்,வெறி நோய்,சுரம்,நாட்பத்ட வளிநோய், குளிர் காய்ச்சல், உடல் வலி, இவை நீங்கும்

வெட்பாலை

பயன்படும் உறுப்பு அரிசி

சுவை - இனிப்பு, தன்மை - தட்பம், பிரிவு - இனிப்பு

செய்கை

உரமாக்கி

குணம்

“வெட்பாலை தன்னரிசி வீறுபித்த வாதமோடு

கொட்பார் கரப்பான் குடல்வாத- உப்பிசத்தைக்

காணாம லேநாளுங் கண்டிக்குங் காசினியிற்

பூணார் முலையா புகழ்”

பொருள்: தீ வளி நோய்கள் , குடல் வாயு, வயிற்று பொருமல் கழிச்சல் போக்கும்

❖ **வாலுளுவை**

பயன்படும் உறுப்பு: விதை

சுவை - கைப்பு, தன்மை - வெப்பம், பிரிவு - கார்ப்பு

செய்கை

- உடற்தேற்றி,
- நாடியுரமாக்கி
- வியர்வை பெருக்கி

குணம்

வயிற்று கடுப்பு, கைகால் குத்தல், குடைச்சல்,கீல் வாயுவில் உண்டாகும் நோக்காடு நீங்கும்

❖ அரத்தை

பயன்படும் உறுப்பு : வேர்,

சுவை - கார்ப்பு, வீரியம் - வெப்பம், பிரிவு - கார்ப்பு

செய்கை

- கோழையகற்றி
- வெப்பகற்றி
- பசித்தீத்தூண்டி

குணம்

வாதசோணிதம்,வீக்கம், தீச்சுரத்தாற் பிறந்த ஐயம், இருமல்,,பல் நோய் போகும்

❖ அதிமதுரம்

பயன்படும் உறுப்பு : வேர்

சுவை - இனிப்பு, தன்மை - சீதம், பிரிவு - இனிப்பு

செய்கை

- வறட்சியகற்றி
- கோழையகற்றி
- மலமிளக்கி
- உரமாக்கி
- உள்ளழலாற்றி

குணம்

எலும்பு பற்றிய நோய் போம், தீக்குற்றத்தின் வன்மயை குறைக்கும், வெறி நோய் விக்கல், வெண்புள்ளி போக்கும்

❖ கோரை

வேறுபெயர் : முத்தக்காசு

பயன்படும் உறுப்பு : கிழங்கு

செய்கை

- துவர்ப்பி

- உரமாக்கி
- சிறுநீர் பெருக்கி
- வியர்வை பெருக்கி
- ருதுவுண்டாக்கி
- புழுவகற்றி

குணம்

சுரம், கழிச்சல், முப்பிணி,பித்த தாகம், கபரோகம்,குதிங்கால் வாதம், வாந்தி, முதலியவை குணமாக்கும்

❖ **கோஷ்டம்**

பயன்படும் உறுப்பு : வேர்

சுவை - கைப்பு, தன்மை - வெப்பம், பிரிவு - கார்ப்பு

செய்கை

- பசித்தீத்தூண்டி
- கோழையகற்றி
- உரமாக்கி
- வெப்பமுண்டாக்கி
- வியர்வை பெருக்கி

குணம்

கண், தாடை, வயிறு, கழுத்து, தலை, நா, வாய், இவ்விடத்தில் உண்டாகும் நோய்கள் குணமாகும்,,சுரம், வாயு,மூலமுளை, இரைப்பிருமல், எலி, பாம்பு, நஞ்சு போக்கும்,

❖ **காட்டுமிளகு**

பயன்படும் உறுப்பு : விதை

சுவை - கார்ப்பு, தன்மை - வெப்பம், பிரிவு -கார்ப்பு

செய்கை

- வெப்பமுண்டாக்கி
- அகட்டுவாய்வகற்றி

குணம்

நாட்பட்ட கழிச்சல், ஐயவளி சுரம்,மேகம், போகும், பசி உண்டாகும்

❖ **அன்னாசிப்பூ**

பயன்படும் உறுப்பு : பூ

சுவை - இனிப்பு, விறுவிறுப்பு, தன்மை -வெப்பம், பிரிவு -கார்ப்பு

செய்கை

- உரமாக்கி
- பசித்தீத்தூண்டி
- வெப்பமுண்டாக்கி

குணம்

செரியாமை, மாந்தம்,வன்மை குறைவு முதலிய நோய்களைப் போக்கும்

❖ குரோசானியோமம்

பயன்படும் உறுப்பு : விதை

சுவை - கார்ப்பு, சிறு கைப்பு, தன்மை - வெப்பம், பிரிவு - கார்ப்பு

செய்கை

- உறக்கமுண்டாக்கி
- தாதுவெப்பகற்றி
- துயரடக்கி
- இசிவகற்றி

குணம்

பல்லடி நோய், சூதகவலி, மந்தர இரைப்பு, கழுத்து நோய், நடுக்கம், தூக்கமின்மை, தமரக துடிப்பு ஆகியவை குணமாகும்

❖ செவ்வியம்

இதுவே மிளகின் வேர்

குணம்

“சூலை அருகிசன்னி தொல்லிருமல் ஈளைபித்தம்

மேலைக் குரற்கம்மல் வெங்களநோய் - மூலசுரம்

கவ்வியங்கத் தேறு கனதா வரவிடமுஞ்

செவ்வியங் கொள்ளவிடுந் தேர்”

பொருள்:

சூலை, சுவையின்மை, முப்பிணி, நாட்பட்ட சுரம், நீடித்த இருமல், ஈளை, வெறி, குரற்கம்மல், தொண்டை நோய், எலும்பைப் பற்றி ஏறுகின்ற நஞ்சு ஆகியவை போக்கும்.

EXTERNAL DRUG

- **மா**

  பயன்படும் உறுப்பு : பட்டை

செய்கை

- துவர்ப்பி
- உரமாக்கி
- எட்டிக்கொட்டை
- செய்கை
- அழுகலகற்றி
- உரமாக்கி

குணம்

- வளிக்குற்றத்தை தன்னிலைப்படுத்தும்
- நரம்புகளுக்கு வன்மை தரும்

- **எருக்கு வேர்ப்பட்டை**

செய்கை

- வெப்பகற்றி
- உடற்தேற்றி
- உரமாக்கி
- வியர்வை பெருக்கி

குணம்

இது நாட்பட்ட கீல்வாதம், குட்டம், நீர்க்கோவை,மேகப்பண், முதலியவை போக்கும்

- **சதுரக்கள்ளி**

சுவை - கார்ப்பு, தன்மை - வெப்பம், பிரிவு - கார்ப்பு

செய்கை

“கரப்பான் சொறியுங் கடியுங் கபமும்

உரப்பான் குன்மம் கீழிக்கும்- நிரைப்ப்ன

பேதிதருஞ் சீதமென்ற பேச்சகற்றும் பூவுலகிற்

ஓது சதுரக்கள்ளி தான்”

ANNEXURE - II

QUALITATIVE AND QUANTITATIVE ANALYSIS

BIO-CHEMICAL ANALYSIS OF MATHIYOOSHNA RASAYANAM

Preparation of the extract:

5gms of the drug was weighed accurately and placed in a 250ml clean beaker. Then 50ml of distilled water is added and dissolved well. Then it is boiled well for about 10 minutes. It is cooled and filtered in a 100ml volumetric flask and then it is make up to 100ml with distilled water. This fluid is taken for analysis.

QUALITATIVE ANALYSIS

S.NO	EXPERIMENT	OBSERVATION	INFERENCE
1.	**TEST FOR CALCIUM** 2ml of the above prepared extract is taken in a clean test tube. To this add 2ml of 4% Ammonium oxalate solution	white precipitate is formed	**presence of calcium**
2.	**TEST FOR SULPHATE** 2ml of the extract is added to 5% Barium chloride solution.	A white precipitate is formed	Presence of sulphate
3.	**TEST FOR CHLORIDE** The extract is treated with silver nitrate solution	No white precipitate is formed	Absence of chloride
4.	**TEST FOR CARBONATE** The substance is treated with concentrated Hcl.	No Brisk effervessence is formed	Absence of carbonate
5.	**TEST FOR STARCH** The extract is added with weak iodine solution	Blue colour is formed	**Indicates presence of starch**
6.	**TEST FOR FERRIC IRON** The extract is acidified with Glacial acetic acid and potassium ferro	No blue colour is formed	Absence of ferric iron

	cyanide.		
7.	**TEST OF FERROUS IRON** The extract is treated with concentrated Nitric acid and Ammonium thio cyanate solution	Blood red colour is formed	**Indicates the presence of ferrous iron**
8.	**TEST FOR PHOSPHATE** The extract is treated with Ammonium Molybdate and concentrated nitric acid	No yellow precipitate is formed	Absence of phosphate
9.	**TEST FOR ALBUMIN** The extract is treated with Esbach's reagent	No Yellow precipitate is formed	Absence of Albumin
10.	**TEST FOR TANNIC ACID** The extract is treated with ferric chloride.	Blue black precipitate is formed	**Indicates the presence of tannic acid**
11.	**TEST FOR UNSATURATION** Potassium permanganate solution is added to the extract	It gets decolourised	**Indicates the presence of unsaturationcompound**
12.	**TEST FOR THE REDUCING SUGAR** 5ml of Benedict's qualitative solution is taken in a test tube and allowed to boil for 2 mts and add 8-10 drops of the extract and again boil it for 2 mts.	Colour change occurs.	**Indicates the presence of Reducing sugar**
13.	**TEST FOR AMINO ACID** One or two drops of the extract is placed on a filter paper and dried well. After drying, 1% Ninnhydrin is sprayed over the same and dried it well.	Violet colour is formed	Presence of Amino acid

14.	**TEST FOR ZINC** The extract is treated with Potassium Ferrocyanide.	No white precipitate is formed	Absence of Zinc.

Inference:

The given sample of "Mathiyooshna Rasayanam contains calcium, ferrous iron, tannic acid, unsaturated compound, reducing sugar, amino acid,Sulfate.

EFFECT OF MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE ON CARRAGEENAN-INDUCED LOCALISED INFLAMMATORY PAIN IN RATS

SUMMARY

The study plan was developed based on the guidelines of Vogel[1] and also it has reference to Chao Ma and Jun-Ming Zhang[2] and Walker et al. [3,] Winter CA, Risley EA, Nuss GW. Carrageenin induced edema in hind paw of the rat as an assay for anti-inflammatory drugs. Proc Soc Exp Biol Med. 1962;111:544–7.

Objective

To study the anti-inflammatory effect of **MATHIYOOSHNA RASAYANAM** were prepared **WITH HONEY/GHEE** in the rat model of Carrageenan-induced localized inflammation.

Methods:

Test System

Species	:	Rat
Strain	:	Albino Wister
Age	:	6-8 weeks at the time of dosing
Total no. of Rats	:	24
Sex	:	Male
Weight	:	150 gm

The animals were housed in polypropylene cages with stainless steel top grills having facilities for holding pellet food and drinking water in bottle with stainless steel sipper tube. Each cage contained 6 rats. All rats had free access to potable water and standard pelleted laboratory animal diet *ad libitum*. Paddy husk was used as bedding material. The animals were divided into 5 groups (6 rats/group). Localized inflammatory pain was induced in all groups of animals by intraplantar injection of carrageenan (50 µl of 3% suspension).

One day before the experiment, three basal readings of hind paw in each rat were recorded. Group 1 received vehicle orally, Group 2 received a standard drug Diclofenac sodium (10 mg/kg i.p), whereas groups 3,4and 5 received **MATHIYOOSHNA RASAYANAM**. The doses of **MATHIYOOSHNA RASAYANAM** were prepared **WITH HONEY/GHEE**, whereas Diclofenac sodium was dissolved in normal saline. After 30 min, the rats were challenged with subcutaneous injection of 0.1 ml of 1% w/v solution of carrageenan into the sub plantar region of left paw. The paw was marked with ink at the level of lateral malleolus and immersed in mercury up to the mark. The paw volume was measured at 0, 1, 2, 3, 4, 5 and 6^{th} hr after carrageenin injection using Digital Plethysmometer. The difference between initial and subsequent reading gave the actual edema volume.

DOSAGE SCHEDULE:

The required dose for mice/rat will be calculated by using the standard dose calculation procedure from recommended clinical dose.

CONVERSION FORMULA:

Human dose is 6000 mg /kg day

Total clinical dose (a) x conversion factor (b) 0.018 = (c) per 150 gm of Rat

6000 mg x 2(a) x 0.018 (b) = 108 (c) /150 gm of Rat

108/1000x150 = 16.2 mg

Experimental Doses Calculated as per the standard procedures are

S.No	Groups	Dose /kg, weight	Volume of administration
1	Vehicle Control	--	1 ml
2	Therapeutic Dose	16.2 mg /kg	1 ml
3	Middle Dose	81mg/kg	1 ml
4	High Dose	405mg/kg	1 ml

EXPERIMENTAL DESIGN:

Group-I: Served as a negative control (0.1ml of 1% carrageenin)

Group-II: Served as standard received Diclofenac sodium (10mg/kg, i.p) +

(0.1ml of 1% carrageenin)

Group-III: Received **MATHIYOOSHNA RASAYANAM** were prepared **WITH HONEY/GHEE**

(16.2 mg /kg) + (0.1ml of 1% carrageenin)

Group IV: Received **MATHIYOOSHNA RASAYANAM** were prepared **WITH HONEY/GHEE**

(81 mg/kg) + (0.1ml of 1% carrageenin)

Group V: Received **MATHIYOOSHNA RASAYANAM** were prepared **WITH HONEY/GHEE**

(405 mg/kg) + (0.1ml of 1% carrageenin)

TABLE: EFFECT OF MATHIYOOSHNA RASAYANAM were prepared WITH HONEY/GHEE ON CARRAGEENIN-INDUCED PAW EDEMA IN RATS (BODY WEIGHT)

Group	Control	Carrageenin + Standard	Carrageenin + LD	Carrageenin + M D	Carrageenin + H D
INITIAL BODY WEIGHT	161.3±3.198	171.5±1.708	165.8±1.652	161.8±2.78	152.3±2.25

Values are expressed as the mean ± S.D. Statistical significance (p) calculated by one way ANOVA followed by dunnett's. ns- not significant $^{**}P< 0.05$ calculated by comparing treated group with control group.

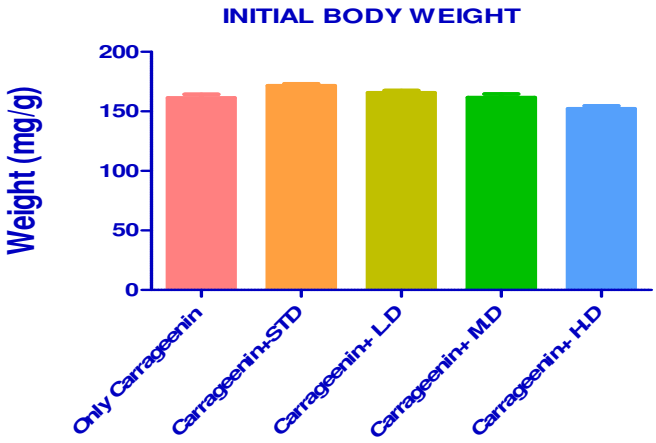


TABLE: EFFECT OF MATHIYOOSHNA RASAYANAM were prepared WITH HONEY/GHEE ON CARRAGEENIN-INDUCED PAW EDEMA IN RATS

Group	Mean paw volume before carrageenan injection	Paw Volume after induction with carrageenin Increase in paw volume (ml) after carrageenan injection (mean ± SEM)/Percent inhibition of edema						
	0 min	30 min	1h	2h	3h	4h	5h	6h
Control Carrageenin	4.588± 0.4256	7.75± 0.5439	7.765± 0.2884	8.315± 0.2375	8.343± 0.1365	8.33± 0.4573	8.028± 0.2207	7.965± 0.2984
Carrageenin **+Standard**	3.75± 0.2779	7.323± 0.2648	7.653± 0.1554	7.763± 0.2521	7.695± 0.1508	6.42± 0.1922**	7.018± 0.1832*	6.023± 0.5354*
Carrageenin + LD	4.213± 0.606	7.898± 0.34	8.125± 0.4637	7.878± 0.2395	8.075± 0.07665	7.455± 0.4548	6.76± 0.3905*	6.308± 0.6038
Carrageenin + M D	3.788± 0.0838	7.73± 0.4115	8.028± 0.5725	7.735± 0.1989	7.838± 0.2671	6.143± 0.3342**	6.238± 0.4052**	6.13± 0.4716
Carrageenin + H D	3.975± 0.3172	7.595± 0.5804	8.2± 0.485	7.33± 0.2054	7.503± 0.1944	6.943± 0.1603	6.305± 0.1455	5.665± 0.35

Values are expressed as the mean ± S.D. Statistical significance (p) calculated by one way ANOVA followed by dunnett's. ns- not significant $^{**}P< 0.05$ calculated by comparing treated group with control group.

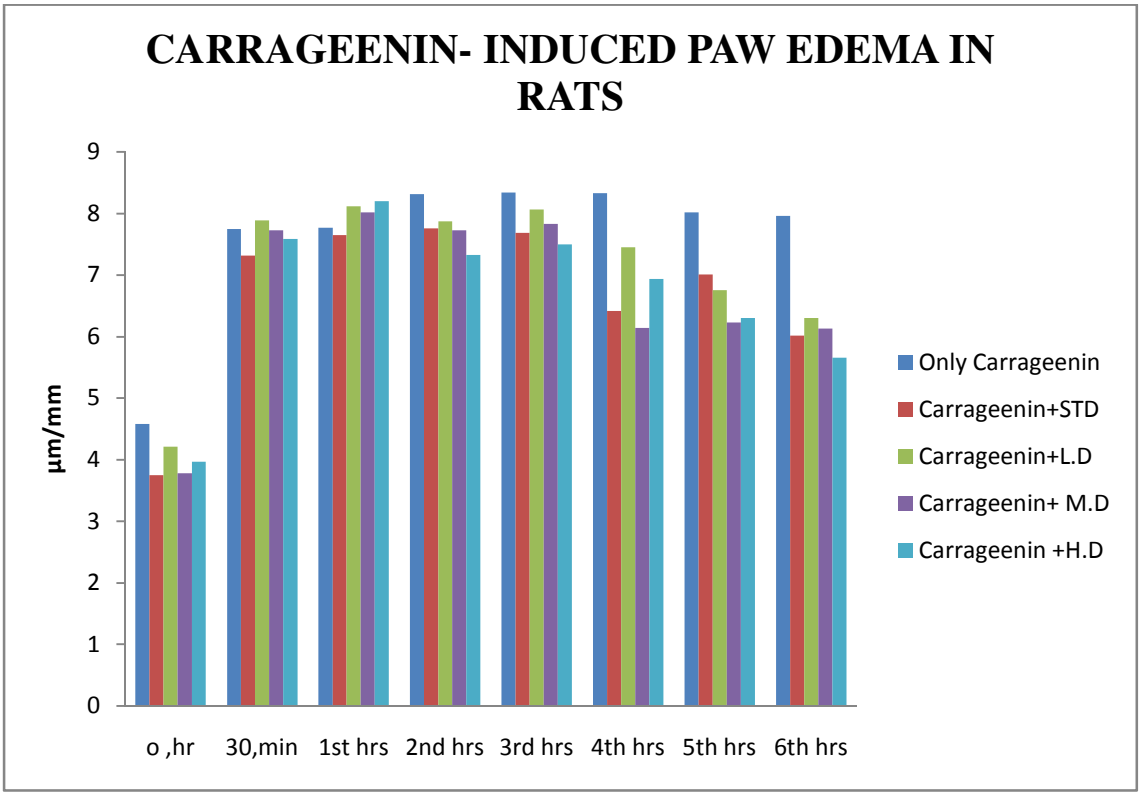

CARRAGEENIN- INDUCED PAW EDEMA IN RATS
µm/mm
9
8
7
6
5
4
3
2
1
0
o ,hr
30,min
1st hrs
2nd hrs
3rd hrs
4th hrs
5th hrs
6th hrs
Only Carrageenin
Carrageenin+STD
Carrageenin+L.D
Carrageenin+ M.D
Carrageenin +H.D

FIGURE SHOWS EFFECT OF MATHIYOOSHNA RASAYANAM were prepared WITH HONEY/GHEE ON CARRAGEENIN-INDUCED PAW EDEMA IN RATS

Only Carrageenin

Carrageenin + STD

Carrageenin + MR L.D

Carrageenin + MR M.D

Carrageenin + MR H.D

EFFECT OF MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE ON ACETIC ACID INDUCED WRITHING IN MICE[1]

1. Kaneria MS, Naik SR, Kohli RK. Anti-inflammatory,antiarthritic and analgesic activity of a herbal formulation. Indian J.Experimental Biol. 2007; 45: 279.

Acetic acid induced writhing method was adopted for evaluation of analgesic activity. Writhing is defined as a stretch, tension to one side, extension of hind legs, contraction of the abdomen so that the abdomen of mice touches the floor, turning of trunk (twist). Any writhing is considered as a positive response.

MATERIAL AND METHODS

ANIMALS:

Healthy Swiss albino rats of either sex weighing 20-25g were used in this study. All the animals were obtained from Animal house of the KMCH College of Pharmacy, Coimbatore. The animals were housed comfortably in a group of six in a single clean plastic cage with a metal frame lid on its top. They were housed under standard environmental conditions of temperature (24±1°C) and relative humidity of 30-70 %. A 12:12 h light dark cycle was followed. All animals had free access to water and standard pelletized laboratory animal diet ad libitum. All the experimental procedures and protocols used in this study were reviewed and approved via the Approval No. ---------- by the Institutional Animal Ethical Committee (IAEC) of KMCH College of Pharmacy, Coimbatore (685/PO/Re/S/2002/CPSCEA Dated 21st August 2002 constituted in accordance with the guidelines of the CPCSEA, Government of India.

DRUGS:

Acetic acid (Sigma Chemical Co. Bangalore, India) and Indomethacin were purchased from (Ranbaxy, India). All drugs were dissolved in saline. The different doses of **MATHIYOOSHNA RASAYANAM** were prepared **WITH HONEY/GHEE**. The control group received vehicle as control. All drugs were prepared just before use.

PREPARATION OF ACETIC ACID:

A solution of acetic acid (1% v/v) in distilled water was prepared.

DOSAGE SCHEDULE:

The required dose for mice/rat will be calculated by using the standard dose calculation procedure from recommended clinical dose.

CONVERSION FORMULA:

Human dose is 6000 mg /kg day

Total clinical dose (a) x conversion factor (b) 0.018 = (c) per 30 gm of mice

6000 mg x 2(a) x 0.018 (b) = 108 (c) /30 gm of mice

108/1000x30 = 3.24 mg

Experimental Doses Calculated as per the standard procedures are

S.No	Groups	Dose /kg, weight	Volume of administration
1	Vehicle Control	--	0.5 ml
2	Therapeutic Dose	3.24 mg /kg	0.5 ml
3	Middle Dose	16.2mg/kg	0.5 ml
4	High Dose	81mg/kg	0.5 ml

EXPERIMENTAL PROCEUDRE:

GROUP 1 – CONTROL (IP injection of 0.1 ml 1% acetic acid)

GROUP 2 -- IP injection of 0.1 ml 1% acetic acid + Indomethacin (5mg/kg, i.p)

GROUP 3 -- 0.1 ml 1% acetic acid (ip) + MATHIYOOSHNA RASAYANAM with HONEY/GHEE
3.24MG /KG(PO)

GROUP 4 -- 0.1 ml 1% acetic acid (ip) + MATHIYOOSHNA RASAYANAM with HONEY/GHEE
16.2mg/Kg(Po)

GROUP 5 -- 0.1 ml 1% acetic acid (ip) + MATHIYOOSHNA RASAYANAM with HONEY/GHEE
81mg/kg(po)

PROCEDURE:

Wister albino mice of either sex were divided into five different groups each containing Six animals, the animals were marked individually. Food was withdrawn 12 hours prior to drug administration till completion of experiment. The animals were weighed and numbered appropriately. The test and standard drugs were given orally. After 60 minutes writhing was induced by intra-peritoneal injection of 1% acetic acid in volume of 0.1 ml/10g body weight. The writhing episodes were recorded for 30 minutes; stretching movements consisting of arching of the back, elongation of body and extension of hind limbs were counted.

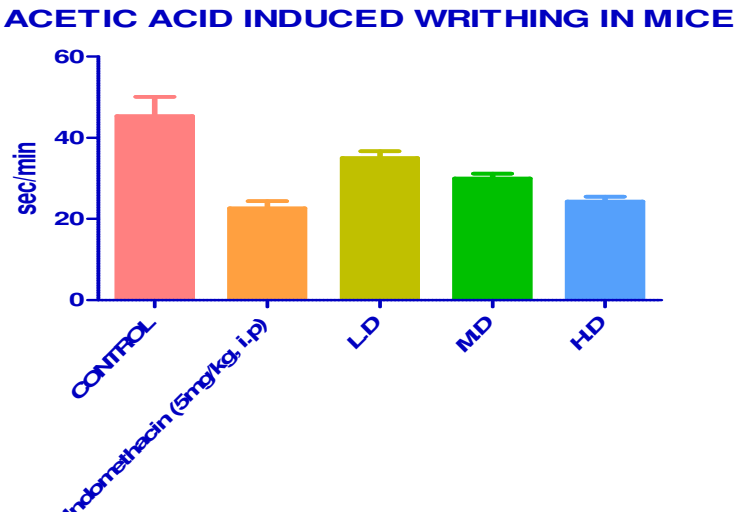
Anti-nociceptive activity was expressed as the percentage inhibition of abdominal constrictions using the ratio:

(Control mean – Treated mean) × 100/Control mean

EFFECT OF MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE ON ACETIC ACID INDUCED WRITHING IN MICE[1]

GROUP	No of Writhing (30min)	Inhibition (%)
CONTROL	45.33±4.807	----
Indomethacin (5mg/kg, i.p)	22.67±1.764	49.98 %
M R 0.028mg/kg(po)	35±1.732	22.78 %
M R 0.014mg/kg(po)	30±1.155	33.81 %
MR 0.28mg/kg(po)	24.33±1.202	46.32 %

Values are expressed as the mean ± S.D; Statistical significance (p)calculated by one way ANOVA followed by dunnett's ns- no significant $^{*}P< 0.001$, $^{**}P < 0.01$, $^{***}P < 0.05$ calculate by comparing treated group with CONTROL group.



EFFECT OF MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE ON HOT PLATE METHOD IN MICE[1]

1. Turner RA. Screening methods in pharmacology. In: Turner, R., Hebborn, P. (eds.). Academic press, New York. 1965; 100.

The paws of mice and rats are very sensitive to heat at temperatures which are not damaging the skin. The responses are jumping, withdrawal of the paws and licking of the paws.

MATERIAL AND METHODS

ANIMALS:

Healthy Swiss albino rats of either sex weighing 20-25g were used in this study. All the animals were obtained from Animal house of the KMCH College of Pharmacy, Coimbatore. The animals were housed comfortably in a group of six in a single clean plastic cage with a metal frame lid on its top. They were housed under standard environmental conditions of temperature (24±1°C) and relative humidity of 30-70 %. A 12:12 h light dark cycle was followed. All animals had free access to water and standard pelletized laboratory animal diet ad libitum. All the experimental procedures and protocols used in this study were reviewed and approved via the Approval No. ---------- by the Institutional Animal Ethical Committee (IAEC) of

KMCH College of Pharmacy, Coimbatore (685/PO/Re/S/2002/CPSCEA Dated 21st August 2002 constituted in accordance with the guidelines of the CPCSEA, Government of India.

The hot plate, which is commercially available, consists of a electrically heated surface. The temperature is controlled for 55° to 56 °C. This can be a copper plate or a heated glass surface. The animals are placed on the hot plate and the time until either licking or jumping occurs is recorded by a stop-watch.

EXPERIMENTAL PROCEUDRE:

GROUP 1 – CONTROL

GROUP 2 – Pentazocine (10mg/kg, I.P)

GROUP 3 -- MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE
3.24 mg /kg(po)

GROUP 4 – MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE
16.2mg/kg(po)

GROUP 5 -- MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE
81mg/kg(po)

PROCEUDRE:

Mice were screened by placing them on a hot plate maintained at 55±1ºC and recording the reaction time in seconds for forepaw licking or jumping. Only mice which reacted within 15sec and which did not show large variation when tested on four separate occasions, each 15min apart, were taken for the test. The time for forepaw licking or jumping on the heated plate of the analgesiometer maintains at 55ºC was taken as the reaction time. Prior to treatment, the reaction time of each mouse (licking of the forepaws or jumping response) was done at 0- and 10-min interval. The average of the two readings was obtained as the initial reaction time (*Tb*). The reaction time (*Ta*) following the administration of the ----------, Pentazocine and distilled water was measured at 0.5, 1, 2, and 3h after latency period of 30min.

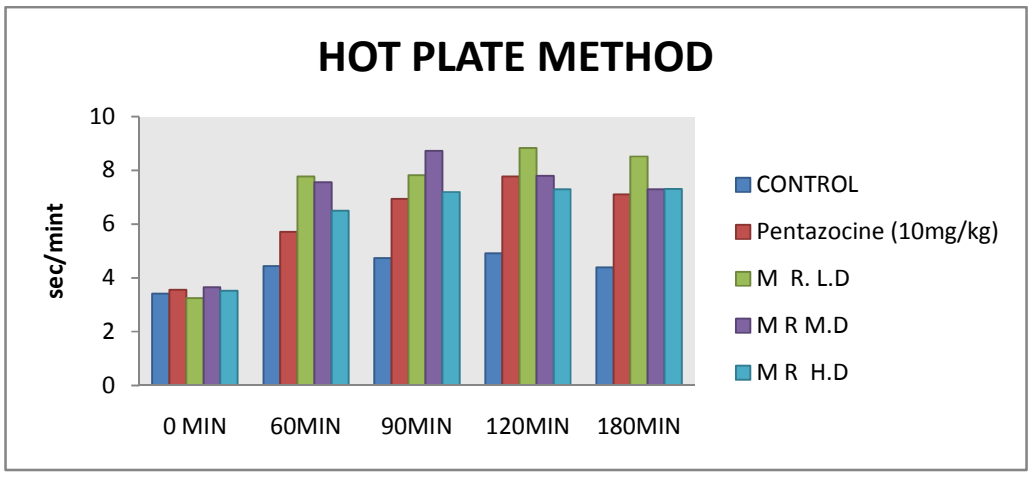
The following calculation was:

Percentage analgesic activity = $Ta\text{-}Tb/Tb \times 100$

EFFECT OF MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE ON HOT PLATE METHOD IN MICE

GROUP	Reaction time in seconds at time (minutes) (mean ± sem) (mean ± sem)				
	O mints	60 mints	90 mints	120 mints	180 mints
CONTROL	3.42±0.14	4.44±0.12	4.745±0.145	4.915±0.045	4.39±0.165
STANDARD	3.56±0.11	5.715±0.065**	6.945±0.055***	7.77±0.02***	7.10±0.21***
M R + LOW DOSE	3.24±0.02	7.77±0.12***	7.82±0.07***	8.83±0.07***	8.52±0.07***
M R + MIDDLE DOSE	3.655±0.095	7.56±0.11***	8.73±0.17***	7.8±0.2***	7.3±0.15***
M R + HIGH DOSE	3.52±0.26	6.5±0.2***	7.2±0.05***	7.3±0.05***	7.31±0.33***

Values are expressed as the mean ± S.D; Statistical significance (p)calculated by one way ANOVA followed by dunnett's $^{***}P< 0.001$, $^{**}P < 0.01$, $^{*}P < 0.05$ calculated by comparing treated group with CONTROL group.



ACUTE TOXICITY STUDY IN FEMALE WISTER RATS TO EVALUATE TOXICITY PROFILE OF MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE

Table 1. Test substance details

Name of the test substance	**VATHATHIRKU LEGHIYAM** **With Honey/Ghee**
Colour of the test substance	- brown
Nature of the test substance	Powder

Table 2. Experimental protocol

Name of the study	Acute toxicity
Guideline followed	OECD 423 method-acute toxic class method
Animals	Healthy young adult female wister rats, nulliparous, non-pregnant
Body weight	150-200 g
Sex	female
Administration of dose and volume	6000 mg/kg in 200g body weight, single dose in 1 ml
Number of groups and animals	5 groups and 3 animals in each group 1000,2000,3000,5000and 6000mg/kg
Route of administration	Oral Cavage (po)
Vechicle	Honey/Ghee

Table3. Housing and feeding conditions

Room temperature	22°C ± 3°C
Humidity	40-60%
Light	12 h : 12h (light : dark cycle)
Feed	Standard laboratory animal food pellets with water *ad libitum*

Table 4. Study period and observation parameters

Initial once observation	First 30 minutes and periodically 24 h
Special attention	First 1-4 h after drug administration
Long term observation	Upto 14 days
Direct observation parameters	Tremors, convulsions, salivation, diarrhea, lethargy, sleep and coma.
Additional observation parameters	Skin and fur, eyes and mucous membrane, respiratory, circulatory, autonomic and central nervous systems, somato motor activity and behavior pattern etc.

The time of death, if any, is recorded. (Complete observations: annexure I). After administration of the drug, food is withheld for a further 1-2 hours.

Study procedure

Acute oral toxicity was performed as per organization for economic co-operation for development (OECD) guideline 423 method. The **MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE** was administered in a single dose by tuberculin syringe. Animals are fasted 3 h prior to dosing (food was withheld for 3 h but not water). Following the period of fasting animals was weighed and test substance was administered orally at a dose of 1000,2000,3000,5000 and 6000mg/kg. After the **MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE** administration, food was withheld 2 h in mice. Animals are observed individually after at least once during the first

30 minutes, periodically during the first 24 hrs, with special attention given during the first 4 hrs, and daily thereafter, for a total of 14 days.

REPORT

Toxicological evaluation of MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE

Table:5 Effect of **MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE** on acute toxicity test in female rats

S.N	Response	Head		Body		Tail	
		Before	After	Before	After	Before	After
1	Alertness	Normal	Normal	Normal	Normal	Normal	Normal
2	Grooming	Absent	Absent	Absent	Absent	Absent	Absent
3	Touch response	Absent	Absent	Absent	Absent	Absent	Absent
4	Torch response	Normal	Normal	Normal	Normal	Normal	Normal
5	Pain response	Normal	Normal	Normal	Normal	Normal	Normal
6	Tremors	Absent	Absent	Absent	Absent	Absent	Absent
7	Convulsion	Absent	Absent	Absent	Absent	Absent	Absent
8	Righting reflux	Normal	Normal	Normal	Normal	Normal	Normal
9	Gripping strength	Normal	Normal	Normal	Normal	Normal	Normal
10	Pinna reflux	Present	Present	Present	Present	Present	Present
11	Corneal reflux	Present	Present	Present	Present	Present	Present
12	Writhing	Absent	Absent	Absent	Absent	Absent	Absent
13	Pupils	Normal	Normal	Normal	Normal	Normal	Normal
14	Urination	Normal	Normal	Normal	Normal	Normal	Normal
15	Salivation	Normal	Normal	Normal	Normal	Normal	Normal
16	Skin colour	Normal	Normal	Normal	Normal	Normal	Normal
17	Lacrimation	Normal	Normal	Normal	Normal	Normal	Normal

RESULT:

From acute toxicity study it was observed that the administration of **MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE** to Female Wister

rats did not induce drug-related toxicity and mortality in the animals up to 6000mg/kg in 200g female Wister rats. So No-Observed-Adverse-Effect- Level (NOAEL) of **MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE** is 6000 mg/kg equal to human dose

DISCUSSION

MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE was administered single time at the doses of 1000,2000,3000,5000 and 6000mg/kg to female Wister rats and observed for consecutive 14 days after administration. Doses were selected based on the pilot study and literature review. All animals were observed daily once for any abnormal clinical signs. Weekly body weight and food consumption were recorded. No mortality was observed during the entire period of the study. Data obtained in this study indicated no significance physical and behavioral signs of any toxicity due to administration of **MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE** at the doses of 1000,2000,3000,5000 and 6000mg/kg to female Wister rats

At the 14th day, all animals were observed for functional and behavioral examination. In functional and behavioral examination, home cage activity, hand held activity were observed. Home cage activities like Body position, Respiration, Clonic involuntary movement, Tonic involuntary movement, Palpebral closure, Approach response, Touch response, Pinna reflex, Sound responses, Tail pinch response were observed. Handheld activities like Reactivity, Handling, Palpebral closure, Lacrimation, Salivation, Piloercetion, Papillary reflex, abdominal tone, Limb tone were observed. Functional and behavioral examination was normal in all treated groups. Food consumption of all treated animals was found normal as compared to normal group.

SUMMARY & CONCLUSION:

Summary:

The present study was conducted to know single dose toxicity of **MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE** on female Wister rats. The study was conducted using 15 female Wister rats. The female animals were selected for study of 8- 12 weeks old with weight range of within ± 20 % of mean body weight at the time of randomisation. The groups were numbered as group I, II, III, IV and V and dose with **1000,2000,3000,5000 and 6000mg/kg** of **LACTIC ACID BACTERIA**. The drug was administered by oral route single time and observed for 14 days. Daily the animals were observed for clinical signs and mortality.

There were no physical and behavioral changes observed in Female Wister rats during 14 days. Mortality was not observed in any treatment groups.

Conclusion:

The study shows that **MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE** did not produce any toxic effect at dose of **1000,2000,3000,5000 and 6000mg/kg** to rats. So No-Observed-Adverse-Effect-Level (NOAEL) of **MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE** is 6000 mg/kg.

7.0 ABBREVIATIONS

No.	Number
Mg	Milligram
Kg	Kilogram
LD_{50}	Lethal Dose $_{50}$
p.o	peros
ML	Milliliter
%	percentage
R&D	Research and Development
g%	Gram percentage
g	Gram
NOAEL	No-Observed-Adverse-Effect-Level

MLD Minimum Lethal Dose
MTD Maximum Tolerated Dose
OECD Organisation of Economic Co-operation and Development
CPCSEA Committee for the Purpose of Control and Supervision of Experiments on Animals

8.0 REFERENCES:

1. OECD. Guideline for Testing of Chemicals 423, Acute oral toxicity (acute toxic class method). December 2001.

SUB-ACUTE TOXICITY STUDY IN WISTER RATS TO EVALUATE TOXICITY PROFILE OF MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE

Objective

The objective of this study is to evaluate the toxic effects, if any, as a result of the repeated once daily oral administration of **MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE** to Wister Albino rats for a minimum period of 28 consecutive days. This study will provide information on any major toxic effects, target organs and a rationale for concluding the No-Observed-Adverse-Effect-Level (NOAEL) and/or No Observed Effect Level (NOEL) / LOEL (Low Observed Effect Level) and risk assessment in humans.

1. Test Guidelines

This study plan is prepared as per the following guidelines:

Schedule – Y, Amendment version 2005, Drugs and Cosmetics Rules, 1945.

OECD – 407 – Repeated dose 28-day Oral Toxicity Study in Rodents, Adopted 3 October, 2008.

1.1. Test System Details

Species	:	Rat
Strain	:	Wister Albino
Source	:	Sree Venkateshwara Enterprises Pvt Ltd, Bangalore
Age	:	6-8 weeks
Sex	:	Male / Female (nulliparous and non-pregnant)
Body weight	:	160.0to 180.0 g

1.2. Acclimatization

Animals will be allowed to acclimatize to the experimental room conditions for five days prior to the commencement of dosing. During the acclimatization period, the animals will be observed daily for any apparent adverse clinical signs. Prior to assignment to the study and commencement of treatment, a detailed physical health examination will be performed on all animals by a veterinarian and animals with any evidence of ill health or poor physical condition will not selected for the study.

1.3. Randomization and Grouping

On the starting day of dosing, the animals will be weighed and health examination will be performed by veterinarian. Animals will be randomly allocated to different groups according to their body weight by using MS-Excel sheet as described in the randomization SOP. Animals will be divided into four groups (vehicle control, low, intermediate, and high dose). At the initiation of the treatment, the body weight variation between the groups did not exceed ±20% of the mean weight of each sex.

1.4. Animal Identification

In each cage, animals will be identified with numbers by marking at the base of the ear. The cages will be identified with an attached colored cage label showing study number, study code, group number, sex, dose, strain, species, cage number, route of administration and animal number.

2. Animal Husbandry

2.1. Animal Welfare and approval

The study was approved by the IAEC (SLS) and Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA registration number: Abc14).Their recommendations regarding animal care and handling will be followed.

2.2. Environmental Conditions

The temperature of the experimental room will be maintained at 22±3^{0}C and the relative humidity between 30-70 %. The photoperiod will be 12 hours light and 12 hours dark cycles

2.3. Housing Conditions

Two animals will be housed in autoclaved polypropylene rat cages (Size in mm=L x W x H: 430 x 290 x 160) using paddy husk as the bedding material. Each cage will be fitted with a top grill having provision for keeping rodent pellet feed and an autoclaved polypropylene water bottle with stainless steel drinking nozzle. Cages will be placed on 3-tier racks and cage rotation will be performed every week. Cages will be changed at least twice a week. The cages and water bottles will be cleaned and autoclave sterilized.

2.4. Sanitation

Each day, the floor of the animal room will be swept and mopped. Cages and bedding material will be changed once in three days and water bottles will be changed daily. All the experimental procedures will be done in a clean environment.

2.5. Feed

The experimental animals will be provided with irradiated rodent pellet feed *ad libitum* supplied from Sai feeds Pvt ltd, Chennai . Feed will be withheld for four hours prior to blood collection and necropsy.

2.6. Drinking Water

Animals will be provided with filtered drinking water *ad libitum* passed through water filter system (Aquaguard™) in autoclaved polypropylene bottles. Water bottles will be changed daily. Microbial analysis of water will be carried out once monthly and the report is maintained in the study file.

3. Personnel Safety

All personnel handling animals undergo regular medical examination. Protective clothing like apron, face mask, head cap, and gloves will be used to maintain hygienic conditions.

4. Materials and Methods

4.1. Preparation of Dose formulation

The dose formulation will be prepared under aseptic conditions as per SLS, SOP.

4.2. Route of Administration and Justification

Administration will be by oral gavage, as it is one of the possible routes of exposure.

4.3. Frequency and Duration of Administration

Once daily for 28 consecutive days

4.4. Dosing Procedure

The test item will be administered in once daily by oral gavage using a suitable intubation cannula fitted with a graduated syringe. The scheme of dosing and sacrifice time points are presented in the below below Table.

4.5. Experimental Procedures

All experimental procedures will be performed in accordance with the Study plan and Standard Operating Procedures (SOPs) of SLS.

4.6 DOSAGE SCHEDULE:

The required dose for mice/rat will be calculated by using the standard dose calculation procedure from recommended clinical dose.

CONVERSION FORMULA:

Human dose is 6000 mg /kg day

Total clinical dose (a) x conversion factor (b) 0.018 = (c) per 150 gm of Rat

6000 mg x 2(a) x 0.018 (b) = 108 (c) /150 gm of Rat

108/1000x150 = 16.2 mg

Experimental Doses Calculated as per the standard procedures are

S.No	Groups	Dose /kg, weight	Volume of administration
1	Vehicle Control	--	1 ml
2	Therapeutic Dose	16.2 mg /kg	1 ml
3	Middle Dose	81mg/kg	1 ml
4	High Dose	405mg/kg	1 ml

Experimental Design

Group No.	Group	Dose (mg/kg b.wt /day)	No. of Animals	
			Male	Female
G1	Vehicle control	**HONEY/GHEE**	5	5
G2	Low dose of **VATHATHIRKU LEGHIYAM WITH HONEY/GHEE**	16.2m g /kg	5	5
G3	Intermediate dose **MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE**	81mg/kg	5	5
G4	High dose **MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE**	405mg/kg	5	5

5. Observations

Animals will be observed daily throughout the treatment period at regular intervals. During the treatment period, animals will be observed twice daily for any clinical signs of toxicity, morbidity and mortality. All the surviving animals will be sacrificed at the end of scheduled period and subjected to gross necropsy and histopathological evaluations.

5.1.Clinical Signs

All the animals will be subjected to cage-side (home-cage) observations twice a day for any clinical signs of toxicity, preferably at the same time each day and considering the peak period of anticipated effect. In addition to home cage observations, a detailed clinical examination will be performed once prior to dosing and weekly thereafter during treatment period.

5.2. Morbidity/ Mortality

All animals will be examined twice a day for mortality and signs of morbidity.

5.3. Body Weights

Body weights will be recorded at the beginning of acclimatization, before randomization, there after at weekly intervals and at the time of necropsy.

5.4. Feed Consumption

Feed consumption will be calculated on a weekly basis throughout the study period.

5.5. Hematology and Clinical Biochemistry

Hematology and clinical biochemistry tests will be performed with terminally collected blood samples on day-29 from all animals. Animals will be deprived of feed overnight and blood samples will be collected by tapping the ear for visibility of the vein site and inserted the needle into the marginal ear vein and collected the blood into micro centrifuge tube. Approximately 0.5 ml of blood will be collected in vials containing 1% EDTA (20µl) as an anticoagulant for hematological analysis.

Approximately 2 ml blood will be collected from each animal in micro centrifuge tubes containing 15µl of heparin (19 units) and the plasma will be separated by centrifugation at 4000 rpm for ten minutes at 4^{o}C. The plasma will be stored at -20 ^{o}C ± 2 and used for all clinical chemistry analysis.

5.6. Hematology

Erythrocyte count (RBC), Total Leucocyte count (WBC), Hemoglobin (Hb), Hematocrit (HCT), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC) and Platelet (PLTC).

5.7. Clinical Biochemistry

Glucose, Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Alkaline phosphatase (ALP), Total protein, Albumin, Creatinine, Urea, Cholesterol, Triglycerides, Sodium, Potassium, Calcium, and Chloride.

5.8 Pathology

All animals will be euthanized by CO_2 asphyxiation and subjected to necropsy under the supervision of the veterinary pathologist. Different tissues/organs of thoracic, abdominal and cranial cavities will be examined for any gross pathological changes. Tissues from vehicle control and high dose groups will be subjected to detailed histopathological analysis (Ovaries/ testes, kidneys, liver, lungs). The organs will be fixed using Bouin's (reproductive organs) and 10% neutral buffered formalin (kidneys, liver, spleen, lungs).Processing of tissue will be done by spin tissue processer, embedding of the tissue by tissue embedder. The tissues will be initially trimmed to 10-20µ thickness and later 3-6µ to obtain thinner tissue sections by using rotary microtome. Haematoxylin and Eosin staining will be performed for all tissues.

5.8. Organ Weights

Absolute weights of adrenal glands, brain, ovaries/testes, epididymis/uterus, heart, kidneys, liver, spleen and lungs will be recorded for all the animals after trimming adherent tissue immediately after dissection from the animal. Paired organs will be weighed together. Relative weights of these organs against fasting animal body weights will be calculated and reported.

6. Data Compilation

Data will be summarised in a tabular form showing the number of animals, experimental design, dose groups, dose volume and concentrations, test item and vehicle control details. All findings like clinical signs, mortality and morbidity data, time of death, body weights, feed consumption, clinical signs, and necropsy and pathology observations will be recorded and given in the final report. One original copy of the final report is issued to the sponsor.

7. Statistical Analysis

All the parameters of treated groups of both sex, viz. body weight, feed consumption, organ weights (absolute and relative), biochemical parameters, and hematology parameters will be analyzed using SPSS software, version 16.0 by using one-way ANOVA test with multiple comparison (vehicle controls treated groups) in the study report, and p value < 0.05 is considered as statistically significant.

8. References

1. Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines for Laboratory Animal Facility, The Gazette of India, 1998.
2. Hayes AW, 2000. Principles and Methods of Toxicology, 4th ed., Taylor and Francis, London.
3. Karl-Heinz Diehl, R. H. (2001). A Good Practice Guide to the Administration of Substances and Removal of Blood, Including Routes and Volumes. journal of applied toxicology , 15-23.
4. OECD – 407 - Repeated dose 28-day oral Toxicity Study in Rodents, Adopted October 3, 2008.
5. Schedule – Y, Amendment version 2005, Drugs and Cosmetics Rules, 1945.

MATERIALS AND METHODS

ESTIMATION OF HEMATOLOGICAL PARAMETERS: [1]

Collection of blood for hematological studies

After the treatment period the animals were anaesthetized by ketamine hydrochloride and the blood was collected from Retro-orbital sinus by using capillary into a centrifugation tube which contains EDTA for haematological parameters The haematological parameters like RBC, WBC and Hb percentage, Differential cell count, MCV, MCHC, Hematocrit, MCH, platelet count were estimated by the following procedures.

1. ENUMERATION OF RED BLOOD CELLS: [1] Ramnic 2007)

Reagents : RBC diluting fluid

Procedure:

Using a red blood cell pipette of haemocytometer, well mixed blood was drawn up to 0.5 mark and RBC diluting fluid was taken up to mark II. The fluid blood mixture was shaken and transferred onto the counting chamber. The cells were allowed to settle to the bottom of the chamber for 2 min. See the fluid does not get dried. Using 45X or high power objective the RBC's were counted uniformly in the larger corner squares.

The cells were expressed as number of cells $x10^{12}/l$

2. ENUMERATION OF WBC: [2] John 1972)

Reagents:

Turk's fluid: Turk's fluid was prepared by mixing 2ml of acetic acid with 100 ml of distilled water. To this 10 drop of aqueous methylene blue 3 % w/v) was added. This solution haemolysis the red cells due to acidity so that counting of white cells becomes easy.

Procedure:

Using a white blood cell pipette of haemocytometer, well mixed blood was drawn up to 0.5 mark and WBC diluting fluid was taken up to mark II. The fluid blood mixture was shaken and transferred onto the counting chamber. The cells were allowed to settle to the bottom of the chamber for 2 min. See the fluid does not get dried.

Using 10X or low power objective the WBC's were counted uniformly in the larger corner squares.

The cells were expressed as number of cells/10mm.

3. DIFFERENTIAL LEUCOCYTE COUNT: [3] John 1972)

Reagent:

Leishmann's stain: 150mg of powdered leishmann's stain was dissolved in 133ml of acetone free methanol.

Procedure:

A blood film stained with leishmann's stain was examined under oil immersion and the different types of WBCs were identified. The percentage distribution of these cells was then determined. Smears were made from anticoagulant blood specimens and stained with leishmann's stain. The slides were preserved for counting the number of lymphocytes and neutrophils, per 100 cells were noted.

From the different Leukocyte count and WBC count, absolute lymphocyte and neutrophil count were calculated.

$$\text{Absolute neutrophil count} = \frac{\text{Number of neutrophils}}{100} \times \text{TWBC}$$

$$\text{Absolute lymphocyte count} = \frac{\text{Number of lymphocytes}}{100} \times \text{TWBC}$$

DETERMINATION OF BIOCHEMICAL PARAMETERS:

For assessment of biochemical parameters, blood samples were collected from the animals by puncturing the retro-orbital plexus and centrifuged. The serum collected after centrifugation was analyzed for various biochemical parameters like SGOT, SGPT, ALP,TC.TG,HDL All of the above biochemical parameters were estimated using semi autoanalyzer (Photometer 5010 $_{V5+}$, Germany) with enzymatic kits procured from Piramal Healthcare limited, Lab Diagnostic Division, Mumbai, India.

1. Total Cholesterol (TC)

Principle

Determination of cholesterol is done after enzymatic hydrolysis and oxidation. The colorimetric indicator is quinoneimine, which is generated from 4-aminoantipyrine and phenol by hydrogen peroxide under the catalytic action of peroxidase (trinder's reaction).

$$\text{Cholesterol ester} + H_2O \xrightarrow{CHE} \text{Cholesterol} + \text{Fatty acid}$$

$$\text{Cholesterol} + O_2 \xrightarrow{CHO} \text{Cholesterol-3-one} + H_2O_2$$

$$2H_2O_2 + \text{4- Amino antipyrine} + \text{Phenol} \xrightarrow{POD} \text{Quinonelimine} + 4\ H_2O_2$$

Method

CHOD-PAP: Enzymatic photometric test

Table 6: Reagents

Goods buffer (pH 6.7)	50 mmol/ l
Phenol	5 mmol/l
4-aminoantipyrine	0.3 mmol/l
Cholesterol estrase	> 200 U/l
Cholesterol oxidase	> 100 U/l
Peroxidase	3 KU/l
Standard	(5.2 mmol/l)

Assay procedure

a. 1 ml (1000 µl) of reagent-1 is taken in a 5 ml test tube.
b. Added 0.01 ml (10 µl) of serum.
c. Mixed well and incubated at 37°C for 5 min.
d. Read the test sample.

NORMAL RANGE: < 200 mg/dl in serum.

1. Deeg R, Ziegenhorn J, Kinetic enzymatic method for automated determination of total cholesterol in serum, Clin. Chem., 1983, 29:1798-802.

2. Triglycerides

Principle

Determination of triglycerides (TG) alters enzymatic splitting with lipoprotein lipase. Indicator is quinoneimine which is generated from 4-aminoantipyrine and 4- chlorophenol by hydrogen peroxidase under the catalytic action of peroxidase.

$$\text{Triglycerides} \xrightarrow{\text{LPL}} \text{Glycerol + fatty acid}$$

$$\text{Glycerol + ATP} \xrightarrow{\text{GK}} \text{Glycerol-3-phosphate+ ADP}$$

$$\text{Glycerol-3-phosphate} + O_2 \xrightarrow{\text{GPO}} \text{Dihydroxyaceton phosphate} + H_2O_2$$

$$2H_2O_2 + \text{4- Amino antipyrine + 4- chlorophenol} \xrightarrow{\text{POD}} \text{Quinonelimine + HCL} + 4H_2O_2$$

Method

Colorimetric enzymatic test using glycerol-3-phosphate-oxidase (GPO).

Reagents

Components and concentrations in the test Goods buffer pH 7.2, 50 mmol/ l

Table 7: Reagents

4-chloroPhenol	4 mmol/l
ATP	2 mmol/l
Mg^{2+}	15 mmol/l
Glycerokinase	> 0.4 Kμ/l
Peroxidase	> 2 Kμ/l
Lipoprotein lipase	> 4 Kμ/l
4-aminoantipyrine	0.5 mmol/l
Glcerol-3-phosphate- oxidase	> 1.5Kμ/l
Standard	(2.3 mmol/l)

Assay procedure

a. 1 ml (1000 µl) of reagent-1 is taken in a 5 ml test tube.
b. Added 0.01 ml (10 µl) of serum.
c. Mixed well and incubated at 37°C for 15 min.
d. Read the test sample.

Normal Range: < 200 mg/dl in serum.

1. Cole T.G, Klotzsch S.G, Mcnarmara J, Measurement of triglyceride concentration, In Rifai N, Warnick G.R, Dominiczak M.H, Handbook of lipoprotein testing, Washington:AACC, Press, 1997, 115-26.

3. HDL Cholestrol

Principle

Chylomicrons, VLDL and LDL are precipitated by adding phosphotungstic acid and magnesium ions to the sample. Centrifugation leaves only the HDL in the supernatant. The cholesterol content in it is determined enzymatically.

Method

Phosphotungstic acid precipitation method.

Table 8: Reagents

Phosphotungstic acid	0.55 mmol/l
Magnesium chloride	25 mmol/l

Assay procedure

A. Preparation of supernatant for the HDL-CHL estimation

Added 200 µl of serum to the 500 µl of HDL-Cholesterol precipitating reagent (from HDL kit) in 1.5 ml centrifuge tube and mixed well. Centrifuged the above solution at 4000 rpm for 10 min.

B. Preparation of test sample for the estimation of HDL-Cholesterol

a. Taken 1000 µl of reagent-1 (from cholesterol kit) in a 5 ml test tube.
b. Added, 100 µl of supernatant from above centrifuged solution
c. Mixed well and incubated at 37°C for 15 min.
d. Read the test sample.

Normal Range: > 60 mg/dl in serum.

1. Friedewald W.T, Levy R.T, Frederickson D.S, Estimation of VLDL and LDL cholesterol, Clin. Chem., 1972, 18:499-502.

4. ESTIMATION OF SERUM GLUTAMATE PYRUVATE TRANSAMINASES (SGPT/ ALT)

1. Determination of aspartate aminotransferase (AST)

Aspartate aminotransferase, also known as Glutamate Oxaloacetate Transaminase (GOT) catalyses the transamination of L-aspartate and α keto glutarate to form oxaloacetate and L-glutamate. Oxaloacetate formed is coupled with 2,4- Dinitrophenyl hydrazine to form hydrazone, a brown coloured complex in alkaline medium which can be measured colorimetrically.

Reagents

Buffered aspartate (pH 7.4); 2,4- DNPH reagent; 4N sodium hydroxide; working pyruvate standard; solution I (prepared by diluting 1 ml of reagent 3 to 10 ml with purified water).

Procedure

Rietman and Frankle method was adopted for the estimation of SGOT. (Reitmann S, Frankel S, 1957. A colorimetric method for the determination of serum oxaloacetic and glutamic pyruvate transminases. American Journal of Clinical Pathology.28: 56-63.The reaction systems used for this study included blank, standard, test (for each serum sample) and control (for each serum sample). 0.25 ml of buffered aspartate was added into all the test tubes. Then 0.05 ml of serum was added to the test group tubes and 0.05 ml of working pyruvate standard into the standard tubes. After proper mixing, all the tubes were kept for incubation at 37^{o}C for 60 min, after which 0.25 ml each of 2,4- DNPH reagent was added into all the tubes. Then, 0.05 ml of distilled water and 0.05 ml of each serum sample was added to the blank and the serum control tubes respectively. The mixture was allowed to stand at room temperature for 20 min. After incubation, 2.5 ml of solution I was added to all test tubes. Mixed properly and optical density was measured in a spectrophotometer at 505 nm within 15 min.

The enzyme activity was calculated as:-

AST (GOT) activity in IU/L) = [(Absorbance of test **-** Absorbance of control)/ (Absorbance of standard - Absorbance of blank)] x concentration of the standard

2. Determination of alanine aminotransferase (ALT)

Alanine aminotransferase, also known as Glutathione Peroxidase (GPT) catalyses the transamination of L-alanine and α keto glutarate to form pyruvate and L- Glutamate. Pyruvate so formed is coupled with 2,4 – Dinitrophenyl hydrazine to form a corresponding hydrazone, a brown coloured complex in alkaline medium which can be measured colorimetrically.

Reagents

Buffered alanine (pH 7.4), 2,4–DNPH, 4N sodium hydroxide, working pyruvate standard, solution I (prepared by diluting 1 ml of reagent 3 to 10 ml with purified water).

Procedure

Rietman and Frankle method was dopted for the estimation of SGPT. The reaction systems used for this study included blank, standard, test (for each serum sample) and control (for each serum sample). 0.25 ml of buffered alanine was added into all the test tubes. This was followed by the addition of 0.05 ml of serum into the test group tubes and 0.05 ml of working pyruvate standard into the standard tubes. After proper mixing, all the tubes were kept for incubation at 37^{o}C for 60 minutes, after which 0.25 ml each of 2,4- DNPH reagent was added into all the tubes. Then, 0.05 ml of distilled water and 0.05 ml of each serum sample was added to the blank and the serum control tubes respectively. The mixture was allowed to stand at room temperature for 20 min. After incubation, 2.5 ml of solution **I** was added to all test tubes. Mixed properly and optical density was read against purified water in a spectrophotometer at 505 nm within 15 min.

The enzyme activity was calculated as:- ALT (GPT) activity in IU/L) = [(Absorbance of test **-** Absorbance of control)/ (Absorbance of standard - Absorbance of blank)] x concentration of the standard.

3. Determination of alkaline phosphatase (ALP)

Alkaline phoshatase from serum converts phenyl phosphate to inorganic phosphate and phenol at pH 10.0. Phenol so formed reacts in alkaline medium with 4-aminoantipyrine in presence of the oxidising agent potassium ferricyanide and forms an orange-red coloured complex, which can be measured spectrometrically. The color intensity is proportional to the enzyme activity.

Reagents:

Buffered substrate

Chromogen Reagent

Phenol Standard, 10 mg%

Procedure:

ALP was determined using the method of Kind (Kind PRM, King EJ, 1972. *In-vitro* determination of serum alkaline phosphatase. Journal of Clinical Pathology 7: 321-22\). The working solution was prepared by reconstituting one vial of buffered substrate with 2.2 ml of water. 0.5 ml of working buffered substrate and 1.5 ml of purified water was dispensed to blank, standard, control and test. Mixed well and incubated at 37^0C for 3 min. 0.05 ml each of serum and phenol standard were added to test and standard test tubes respectively. Mixed well and incubated for 15 min at 37^0C. Thereafter, 1 ml of chromogen reagent was added to all the test tubes. Then, added 0.05 ml of serum to control. Mixed well after addition of each reagent and the O.D of blank, standard, control and test were read against purified water at 510 nm.

Serum alkaline phosphatase activity in KA units was calculated as follows
[(O.D. Test-O.D. Control) / (O.D. Standard- O.D. Blank)] x 10

4. Determination of bilirubin

In toxic liver, bilirubin levels are elevated. Hyperbilirubinemia can result from impaired hepatic uptake of unconjugated bilirubin, such a situation can occur in generalized liver cell injury, certain drugs (e.g Rifampin and probenecid) interfere with the rat uptake of bilirubin by the liver cell and may produce a mild unconjugated hyperbilirubinemia. Bilirubin level rises in

diseases of hepatocytes, obstruction to bilirubin excretion into duodenum, in haemolysis and defects of hepatic uptake and conjugation of Bilirubin pigment such as Gilbert's disease.

Elevation of total serum bilirubin may occur due to:

1.Excessive haemolysis or destruction of the red blood cells.Eg:Haemolytic disease of the new born.

2.Liver diseases.Eg.Hepatitis and cirrhosis.

3.Obstruction of the biliary tract.Eg.Gall stones.

The method is based on the reaction of Sulfonilic acid with sodium nitrite to form azobilirubin which has maximum absorbance at 546nm in the aqueous solution. The intensity of the color Produced is directly proportional to the amount of direct or total bilurubin concentration present in the sample.

Reagents

1. Diazo A-(Reagent-R1) :Ready to use
2. Diazo B-(Reagent-R2):Ready to use
3. Bilirubin Activater :Ready to use

Procedure

Kind & King's method was followed for the estimation of Bilirubin. Five hundred µl of working reagent was added to 50 µl of rat serum & incubated for 5 min at 37°C. Absorbance was measured AT 546 NM in semi auto analyzer against the standard.

The Bilirubin content was calculated using the following equation:

Total bilirubin (mg/dt) = Abs of the sample blank x 15.

Direct Bilirubin(mg/dt) = Abs of sample blank x 10.

5. ESTIMATION OF UREA

Urea is the nitrogen-containing end product of protein catabolism. States associated with elevated levels of urea in blood are referred to as hyper uremia or azotemia.

Method

Estimation of urea was done by Urease-GLDH: enzymatic UV test.

Principle

$$\text{Urea} + 2H_2O \xrightarrow{\text{Urease}} 2NH_4 + 2HCO_3$$

$$\text{2- Oxoglutarate} + NH_4^+ + \text{NADH} \xrightarrow{\text{GLDH}} \text{L- Glutamate} + NAD^+ + H_2O$$

Table 14. Reagents

R 1	TRIS pH 7.8	120 mmol/l
	2-Oxoglutarate	7 mmol/l
	ADP	0.6 mmol/l
	Urease	≥ 6 KU/l
	GLDH	≥ 1 KU/l
R 2	NADH	0.25 mmol
R 3	Standard	40 mg/dl

Procedure

a. Take 1000 µl of reagent-1 and 250 µl of reagent-2 in 5 ml test tube.
b. To this, add 10 µl of serum.
c. Mix well and immediately read the test sample at 340 nm Hg 334 nm Hg 365 nm optical path 1 cm against reagent blank (2-point kinetic).
d. And note down the value.

Normal range: 10 – 50 mg/dl.

6. ESTIMATION OF URIC ACID

Uric acid and its salts are end products of the purine metabolism. In gout the most common complication of hyperuricemia, ie. Increased serum levels of uric acid lead to formation of monosodium urate crystal around the joints.

Method

Enzymatic photometric test using TOOS (N ethyl- N (hydroxyl -3- sulfopropyl)-m- toluidin)

Principle

Uric acid + H_2O + O_2 $\xrightarrow{\text{uricase}}$ Allantoin +CO_2 +H_2O_2

TOOS + 4 aminoantipyrine + $2H_2O_2$ $\xrightarrow{\text{POD}}$ Indamine + $3H_2O$

Table 15.reagents

R1	Phosphate buffer pH 7.0	100mmol/l
	TOOS	1mmol/l
	Ascorbate oxidase	≥1 KU/l
R2	Phosphate buffer pH 7.0	100mmol/l
	4- amino antipyrine	0.3mmol/l
	K_4 (Fe(CN)$_6$)	10µmol/l
	Peroxidase	≥1KU/l
	Uricase	≥50U/l

Procedure

a. Take 800µl of reagents -1 in a2ml centrifuge tube.
b. To this add 20µl of serum.
c. Mix well and incubate at 30°c for 5 minutes.
d. Then add 200µl of reagent2
e. Mix well incubate for 5min at 37°c
f. Measure the not down the values.

Normal range: 1.9-8.2mg/dl

7. ESTIMATION OF CREATININE:

Principle:

Creatinine forms a coloured complex with picrate in alkaline medium.

The rate of formation of the complex is measured.

Reagents:

Reagent 1 Standard Creatinine (2mg/100ml)

Reagent 2 Picric acid solution.

Reagent 3 sodium hydroxide solution

Procedure:

Take 500 µl of reagent -2 and 500 µl of reagent -3 in a 5ml test tube. To this add 100 µl of serum. Mix well and immediately read the test sample at Hg 492 nm 1cm light path and note down the values.

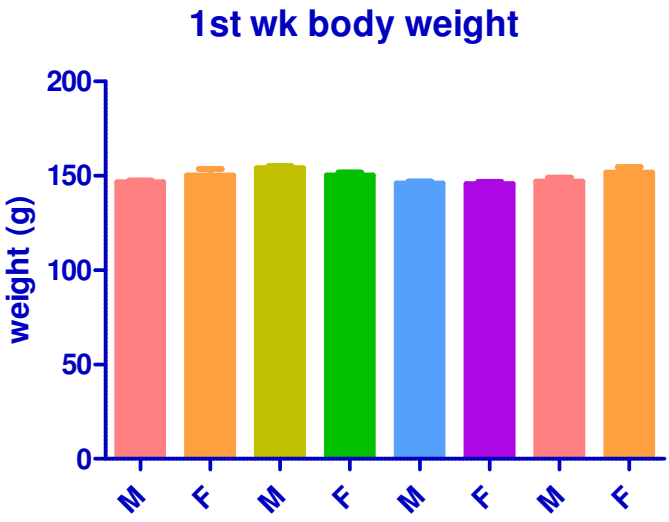
Normal range is 0.6 -1.1 mg/dl.

TABLE: 1 EFFECT OF SUB-ACUTE DOSES (28 DAYS) OF MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE ON BODY WEIGHT IN Gram (PHYSICAL PARAMETER)

EFFECT OF SUB ACUTE DOSES (28 DAY) 0F MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE ON BODY WEIGHT IN Gram (PHYSICAL PARAMETER).

GPs	Control		Low Dose		Middle Dose		High Dose	
	Male	Female	Male	Female	Male	Female	Male	Female
1st wk	146.7± 0.8819	150.3± 3.283	154± 1.155	150.3± 1.453	146± 1.155	145.7± 1.202	147± 2.082	151.7± 2.963
2nd wk	153± 2.082	155±4	159.3± 0.8819	155.3± 1.453	151.7± 1.453	153.3± 2.333	153.3± 2.186	158± 2.887
3rd wk	163.3± 3.712	165± 3.512	166.3± 1.333	166.3± 1.453	160± 3.055	162.3± 1.764	161.3± 1.764	165.3± 3.18
4th wk	171.7± 1.453	172.7± 2.404	174± 2.646	174.3± 0.8819	171.3± 2.186	169.3± 3.756	176.3± 0.8819	173.7± 2.603

Values are expressed as the mean ± S.D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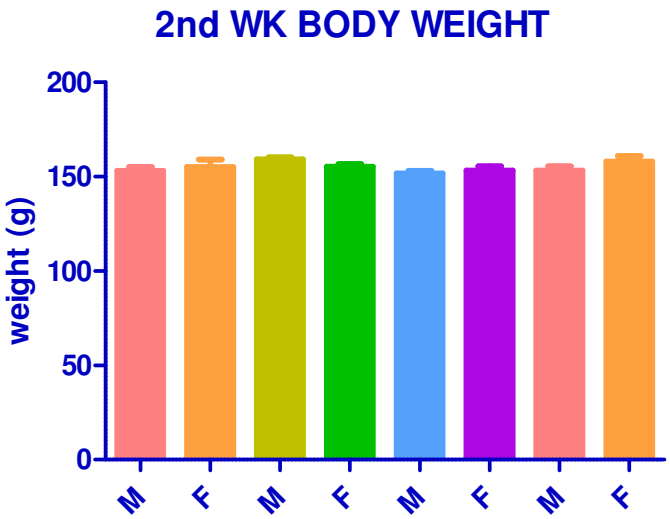
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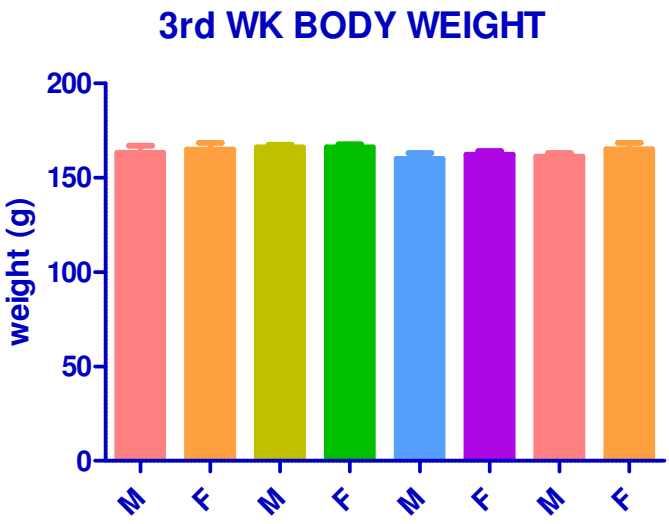
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weight (g)
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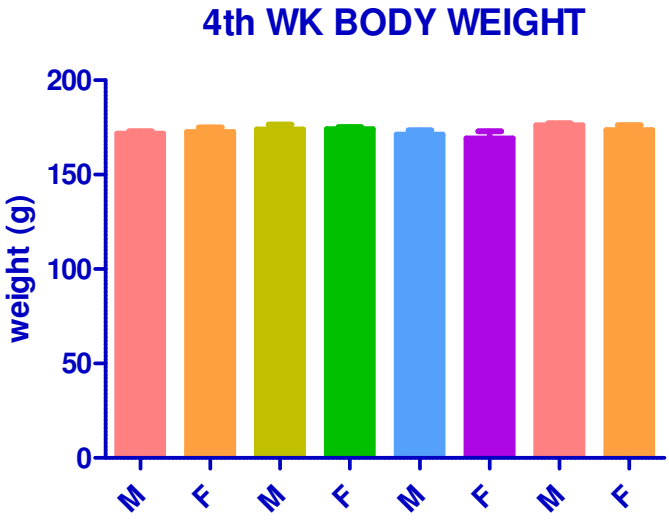
4th WK BODY WEIGHT
weight (g)
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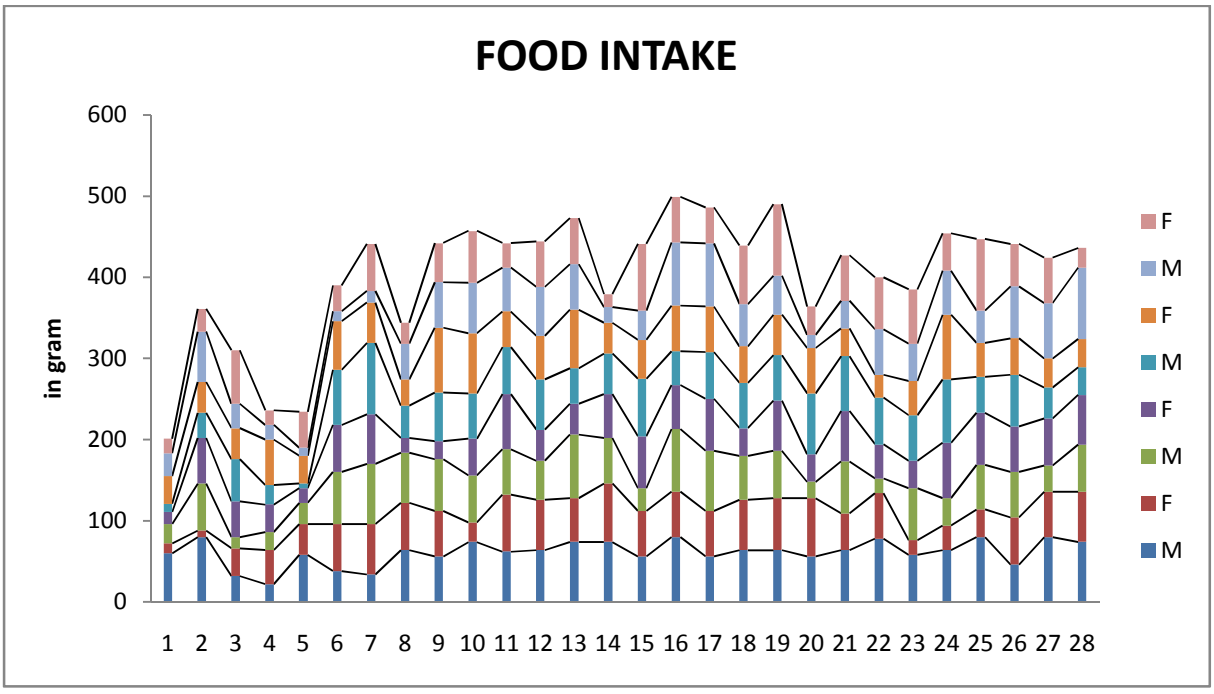
EFFECT OF SUB-ACUTE DOSES (28 DAYS) OF MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE ON FOOD INTAKE In Gram

Effect Of Sub Acute Doses (28 Days) 0f MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE ON FOOD INTAKE IN gms

Groups	Control		Low Dose		Middle Dose		High Dose	
DAY	Male	Female	Male	Female	Male	Female	Male	Female
Day 1	60	12	24	15	10	34	28	18
DAY2	80	8	58	56	31	38	62	28
DAY3	32	34	14	44	52	38	30	66
Day 4	22	42	22	34	24	56	18	18
DAY5	58	38	26	18	6	34	10	44
Day 6	38	58	64	58	68	60	12	32
DAY7	34	62	74	61	88	50	14	58
DAY8	64	58	62	18	40	32	44	26
Day 9	56	56	64	22	60	80	56	48
DAY10	74	24	58	45	56	74	62	64
Day 11	62	70	56	68	58	44	54	30
DAY12	64	62	48	38	62	54	60	56
DAY13	74	54	78	38	44	72	56	57
Day 14	74	72	56	54	50	38	19	16
DAY15	56	56	28	64	71	48	36	82
Day 16	80	56	77	54	42	56	78	56
DAY17	56	56	74	64	58	56	78	44

DAY18	64	62	54	34	56	45	52	72
Day 19	64	64	58	62	56	50	48	88
DAY20	56	72	20	34	75	56	16	35
DAY21	64	45	64	62	68	34	34	56
Day 22	78	56	18	42	58	28	56	64
DAY23	58	18	64	34	56	42	46	67
DAY24	64	30	34	68	78	80	54	46
Day 25	80	34	55	64	44	42	40	88
DAY26	46	58	56	56	64	45	64	52
DAY27	80	56	32	58	38	36	68	56
DAY28	74	62	58	61	34	35	88	24

Values are expressed as the mean ± S.D



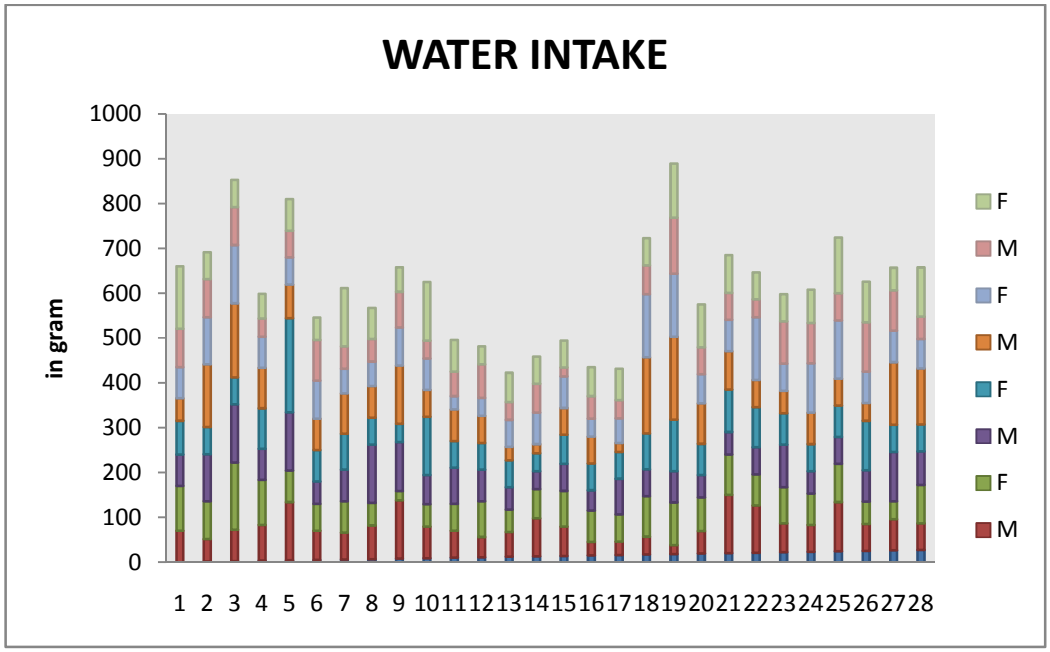
EFFECT OF SUB-ACUTE DOSES (28 DAYS) OF MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE ON WATER INTAKE IN ml

Effect Of Sub Acute Doses (28 Day) 0f MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE on Water Intake in ml

Groups	Control		Low Dose		Middle Dose		High Dose	
DAY	Male	Female	Male	Female	Male	Female	Male	Female
Day 1	70	100	70	75	50	70	85	140
DAY2	50	85	105	60	140	105	85	60
DAY3	70	150	130	60	165	130	85	60
Day 4	80	100	70	90	90	70	40	55
DAY5	130	70	130	210	75	60	60	70
Day 6	65	60	50	70	70	85	90	50
DAY7	60	70	70	80	90	55	50	130
DAY8	75	50	130	60	70	55	50	70
Day 9	130	20	110	40	130	85	80	55
DAY10	70	50	65	130	60	70	40	130
Day 11	60	60	80	60	70	30	55	70
DAY12	45	80	70	60	60	40	75	40
DAY13	55	50	50	60	30	60	40	65
Day 14	85	65	40	40	20	70	65	60
DAY15	65	80	60	65	60	70	20	60
Day 16	30	70	45	60	60	40	50	65
DAY17	30	60	80	60	20	55	40	70

DAY18	40	90	60	80	170	140	65	60
Day 19	20	95	70	115	185	140	125	120
DAY20	50	75	50	70	90	65	60	95
DAY21	130	90	50	95	85	70	60	85
Day 22	105	70	60	90	60	140	40	60
DAY23	65	80	95	70	50	60	95	60
DAY24	60	70	50	60	70	110	90	75
Day 25	110	85	60	70	60	130	60	125
DAY26	60	50	70	110	40	70	110	90
DAY27	70	40	110	60	140	70	90	50
DAY28	60	85	75	60	125	65	50	110

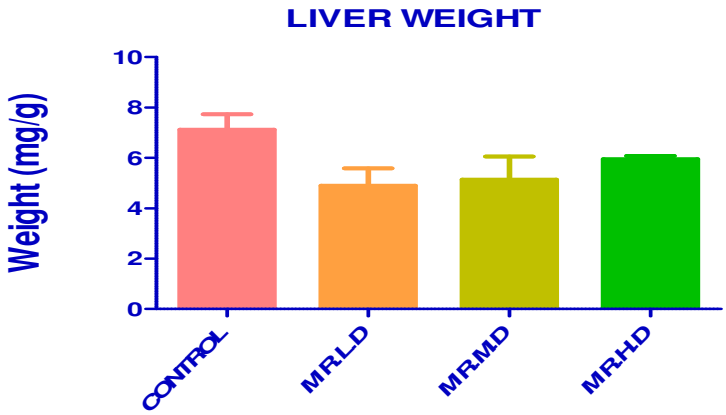
Values are expressed as the mean ± S.D

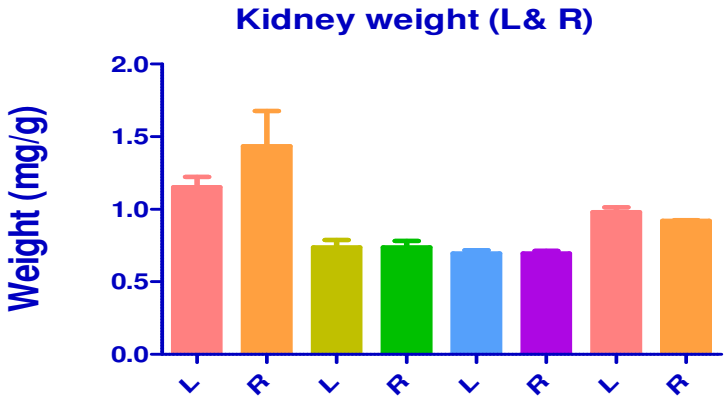


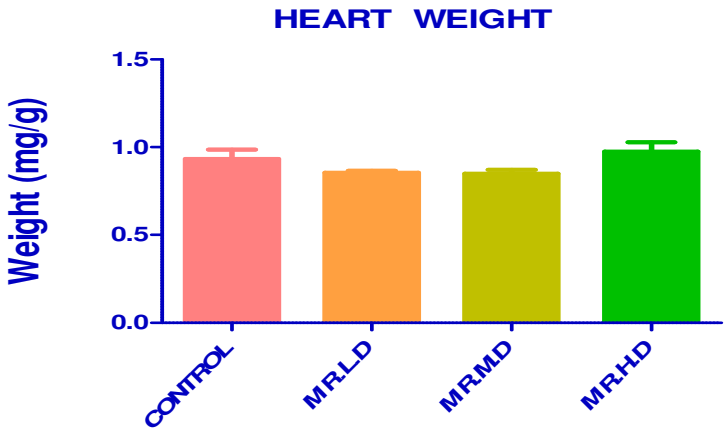
EFFECT OF SUB-ACUTE DOSES (28 DAYS) OF MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE ON ORGAN WEIGHT in gm

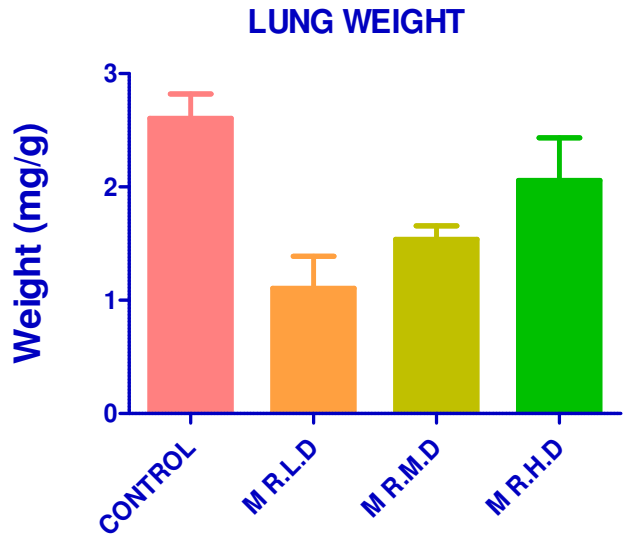
GROUP		CONTROL	Low Dose	Middle Dose	High Dose
LIVER WEIGHT		7.124±0.6045	4.894±0.6955	5.145±0.91	5.955±0.133
KIDNEY WEIGHT	L	1.152±0.07	0.738±0.05	0.696±0.022	0.98±0.032
	R	1.434±0.2445	0.737±0.045	0.6965±0.0175	0.921±0.005
HEART WEIGHT		0.9325±0.0535	0.8555±0.0105	0.85±0.022	0.975±0.053
LUNGS WEIGHT		2.605±0.217	1.107±0.281	1.54±0.116	2.06±0.373
TESTIS WEIGH		2.346±0.021	2.233±0.093	1.831±0.147	1.762±0.2165
UTERUS		0.724±0.068	0.6225±0.0705	0.548±0.114	0.615±0.053

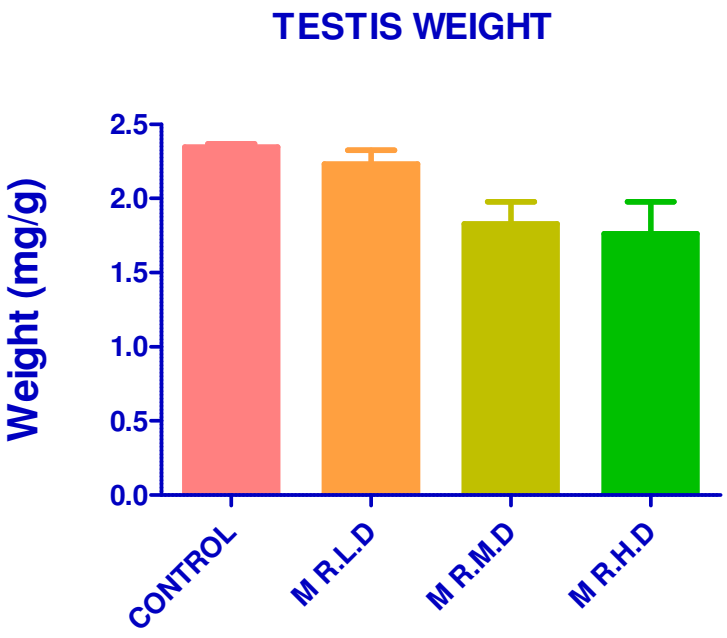
Values arae expressed as mean ± SEM Statistical significance (p) calculated by one way ANOVA followed by dunnett's (n=6); $^{ns}p>0.05$, *p<0.05, **p<0.01, ***p<0.001, calculated by comparing treated groups with control group.

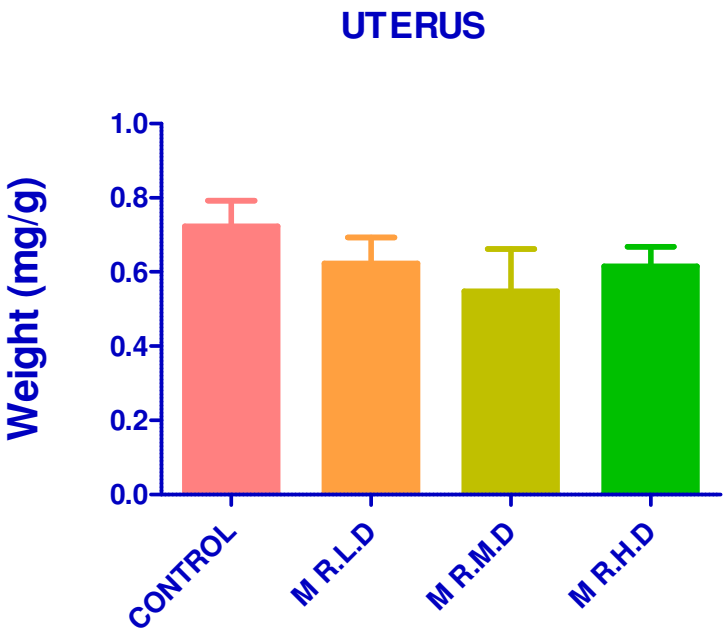



Kidney weight (L& R)
Weight (mg/g)
2.0
1.5
1.0
0.5
0.0
L
R
L
R
L
R
L
R


HEART WEIGHT
Weight (mg/g)
1.5
1.0
0.5
0.0
CONTROL
M.R.L.D
M.R.M.D
M.R.H.D


LUNG WEIGHT
Weight (mg/g)
3
2
1
0
CONTROL
M R.L.D
M R.M.D
M R.H.D

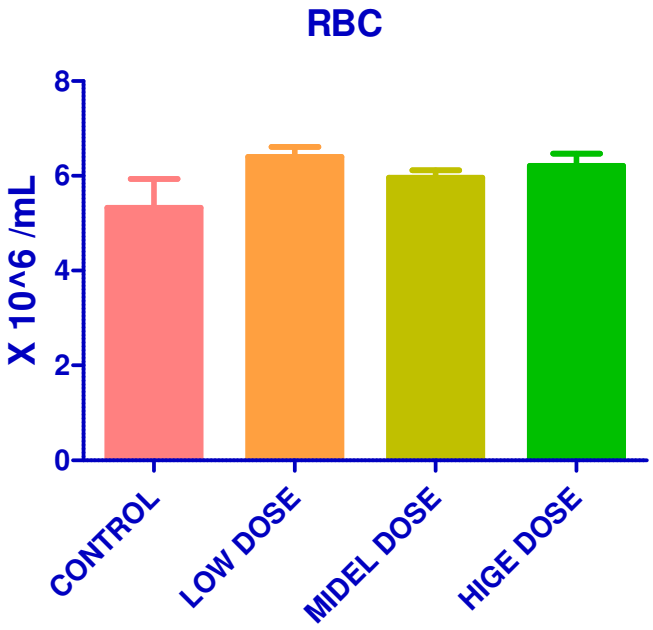

TESTIS WEIGHT
Weight (mg/g)
2.5
2.0
1.5
1.0
0.5
0.0
CONTROL
M R.L.D
M R.M.D
M R.H.D

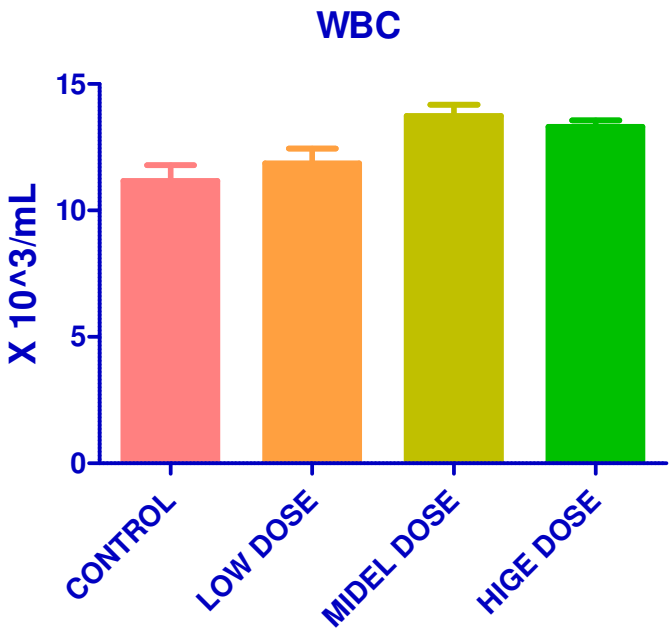

UTERUS
Weight (mg/g)
1.0
0.8
0.6
0.4
0.2
0.0
CONTROL
M R.L.D
M R.M.D
M R.H.D

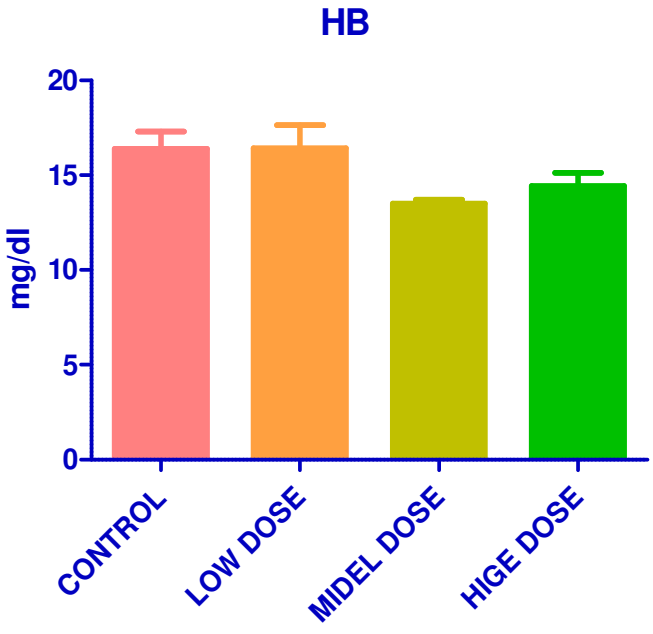
Effect Of Sub Acute Doses (28 Day) 0f MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE On HAEMATOLOGICAL PARAMETERS

Groups	Control	Low Dose	Middle Dose	High Dose
Rbc ($X10^3$/µl)	5.33±0.6071	6.403±0.2043	5.96±0.1537	6.213±0.2559
Wbc($X10^6$/µl)	11.17±0.6196	11.87±0.5807	13.73±0.4497**	13.3±0.255*
Hb (g/dl)	16.4±0.912	16.43±1.209	13.5±0.216	14.43±0.6933

Values are expressed as the mean ± S.D; Statistical significance (p)calculated by one way ANOVA followed by dunnett's ns- no significant $^{*}P< 0.001$, $^{**}P < 0.01$, $^{***}P < 0.05$ calculate by comparing treated group with CONTROL group.



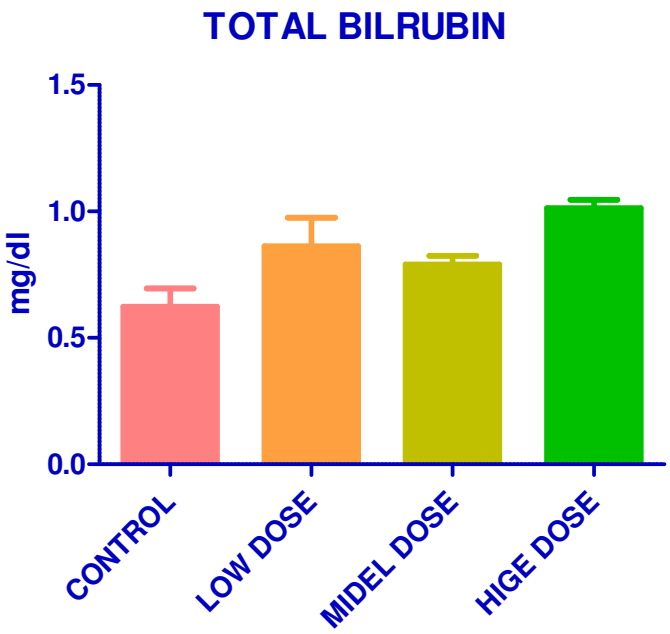

WBC
X 10^3/mL
15
10
5
0
CONTROL
LOW DOSE
MIDEL DOSE
HIGE DOSE


HB
mg/dl
20
15
10
5
0
CONTROL
LOW DOSE
MIDEL DOSE
HIGE DOSE

EFFECT OF SUB ACUTE DOSES (28 DAY) 0F MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE ON BIOCHEMICAL PARAMETER (LIVER PROFILE)

Groups	Control	Low Dose	Middle Dose	High Dose
Total Bilirubin(mg/dl)	0.6233±0.07219	0.8633±0.1126	0.79±0.03464	1.013±0.0318*

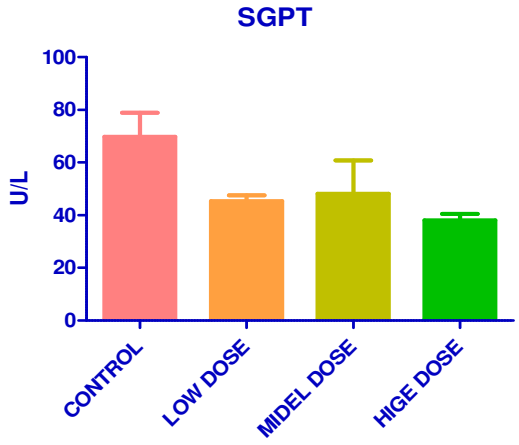
Values are expressed as the mean ± S.D; Statistical significance (p)calculated by one way ANOVA followed by dunnett's ns- no significant $^{*}P< 0.001$, $^{**}P < 0.01$, $^{***}P < 0.05$ calculate by comparing treated group with CONTROL group.

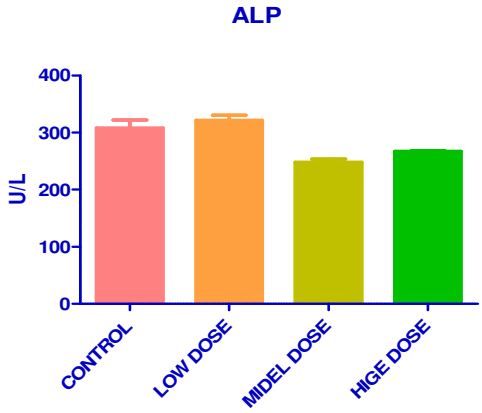


EFFECT OF SUB ACUTE DOSES (28 DAY) 0F MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE ON BIOCHEMICAL PARAMETER (LIVER PROFILE)

Groups	Control	Low Dose	Middle Dose	High Dose
SGOT (U/L)	85.95±5.34	133.2±21.91	77.9±8.603	81.35±1.761
SGPT (U/L)	69.79±9.073	45.4±2.194	48.15±12.62	38.15±2.281
ALP (U/L)	308.2±14.17	321.8±9.093	247.8±6.091	267.3±1.097

Values are expressed as the mean ± S.D; Statistical significance (p) calculated by one way ANOVA followed by dunnett's ns- no significant $^{*}P< 0.001$, $^{**}P < 0.01$, $^{***}P < 0.05$ calculate by comparing treated group with CONTROL group.

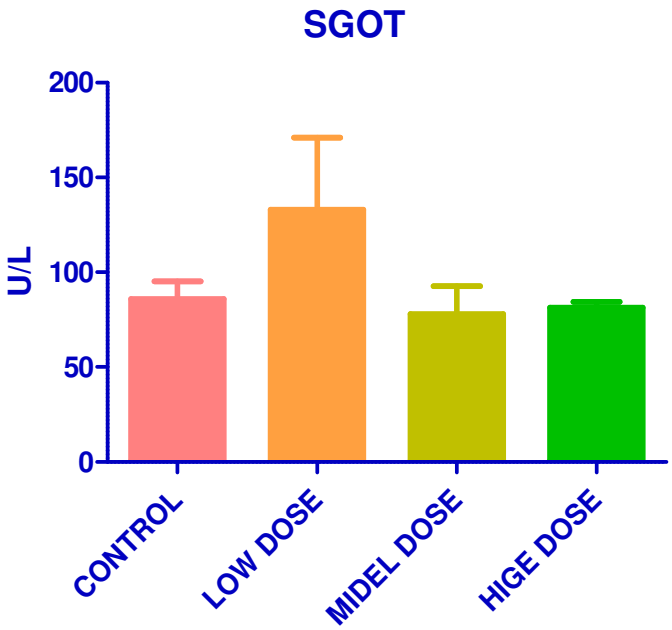


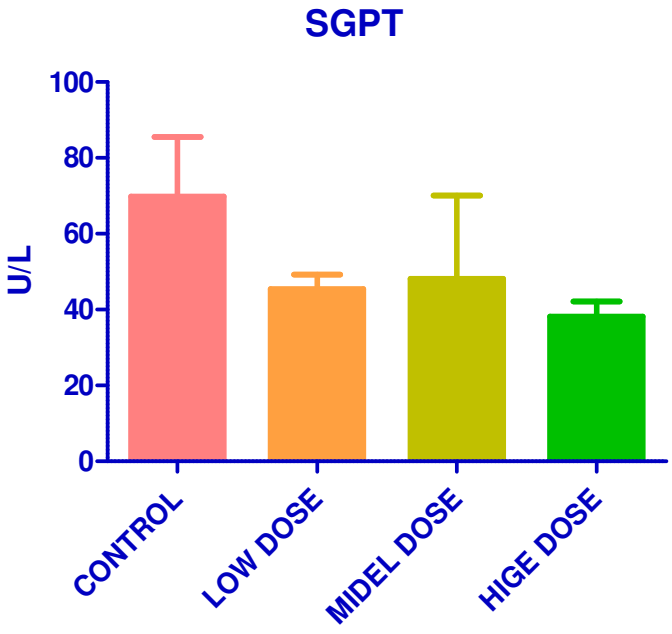


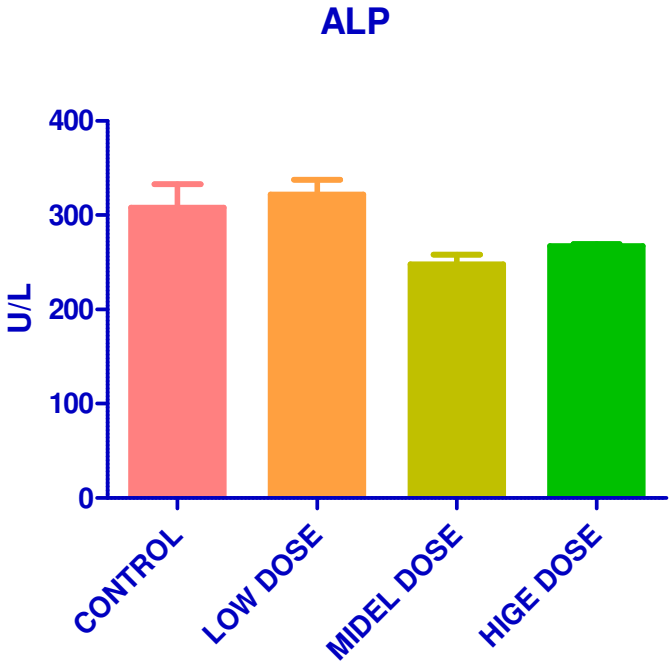
EFFECT OF SUB ACUTE DOSES (28 DAY) 0F MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE ON BIOCHEMICAL PARAMETER (LIVER PROFILE)

Groups	Control	Low Dose	Middle Dose	High Dose
SGOT (U/L)	85.95±9.25	133.2±37.95	77.9±14.9	81.35±3.05
SGPT (U/L)	69.79±15.72	45.4±3.8	48.15±21.85	38.15±3.95
ALP (U/L)	308.2±24.55	321.8±15.75	247.8±10.55	267.3±1.9

Values are expressed as the mean ± S.D; Statistical significance (p) calculated by one way ANOVA followed by dunnett's ns- no significant $^{*}P< 0.001$, $^{**}P < 0.01$, $^{***}P < 0.05$ calculate by comparing treated group with CONTROL group.



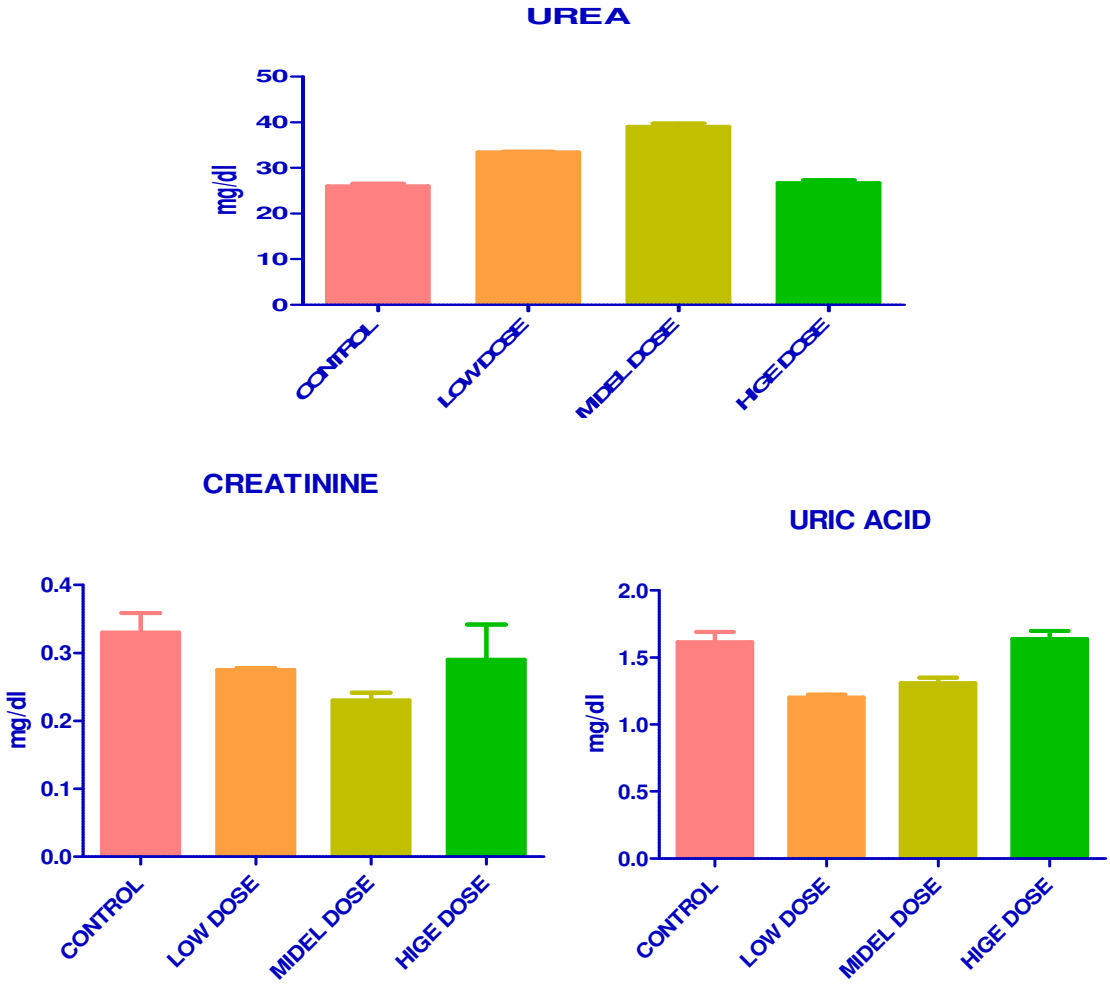

SGPT
100
80
60
40
20
0
U/L
CONTROL
LOW DOSE
MIDEL DOSE
HIGE DOSE


ALP
400
300
200
100
0
U/L
CONTROL
LOW DOSE
MIDEL DOSE
HIGE DOSE

EFFECT OF SUB ACUTE DOSES (28 DAY) 0F MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE ON BIOCHEMICAL PARAMETER (KIDNEY PROFILE)

Groups	Control	Low Dose	Middle Dose	High Dose
Urea (mg/dl)	26.03±0.5831	33.45±0.1443	39.08±0.6813	26.74±0.6524
Uric acid (mg/dl)	1.615±0.07794	1.2±0.02309**	1.31±0.04041**	1.64±0.05774
Creatinine (mg/dl)	0.33±0.02887	0.275±0.002887	0.23±0.01155	0.29±0.05196

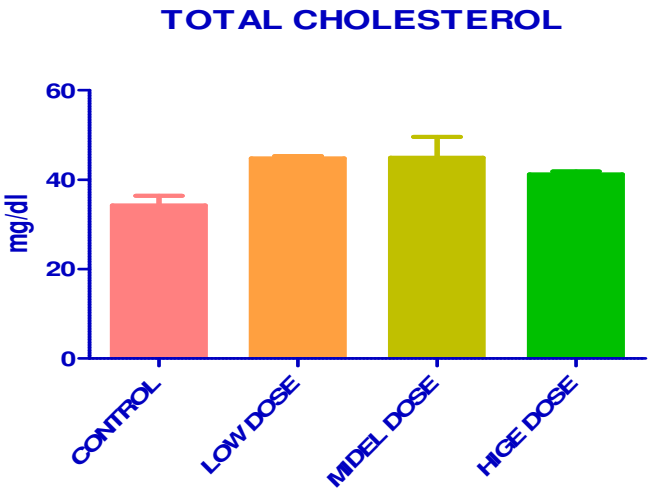
Values are expressed as the mean ± S.D; Statistical significance (p)calculated by one way ANOVA followed by dunnett's ns- no significant $^{*}P< 0.001$, $^{**}P < 0.01$, $^{***}P < 0.05$ calculate by comparing treated group with CONTROL group.

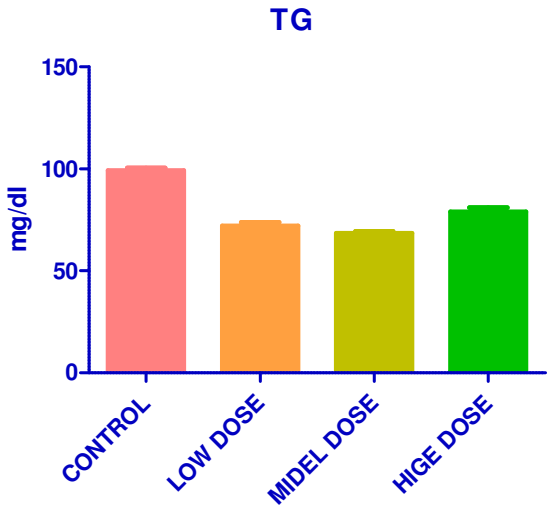


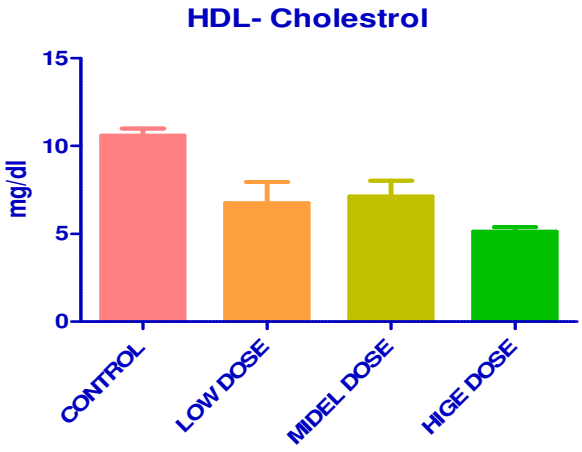
EFFECT OF SUB ACUTE DOSES (28 DAY) 0F MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE ON BIOCHEMICAL PARAMETER (LIPID PROFILE)

Groups	Control	Low Dose	Middle Dose	High Dose
Total cholesterol (mg/dl)	34.3±2.078	44.83±0.4333*	44.93±4.648*	41.2±0.6351
Triglycerides (mg/dl)	99.3±1.225	72.03±1.776***	68.4±1.042***	78.9±2.164***
HDL-Cholesterol (mg/dl)	10.61±0.3955	6.75±1.21*	7.133±0.895*	5.133±0.2603**

Values are expressed as the mean ± S.D; Statistical significance (p)calculated by one way ANOVA followed by dunnett's ns- no significant $^{*}P< 0.001$, $^{**}P < 0.01$, $^{***}P < 0.05$ calculate by comparing treated group with CONTROL group.







RESULTS:

CLINICAL SIGNS:

All animals in this study were free of toxic clinical signs throughout the dosing period of 28 days.

Mortality:

All animals in control and in all the treated dose groups survived throughout the dosing period of 28 days.

Body weight:

Results of body weight determination of animals Table-1 from control and different dose groups exhibited comparable body weight gain throughout the dosing period of 28 days.

Food consumption:

During dosing and the post-dosing recovery period, the quantity of food consumed by animals from different dose groups was found to be comparable with that by control animals.

Organ Weight:

Group Mean Relative Organ Weights (% of body weight) are recorded in Table No.4 Comparison of organ weights of treated animals with respective control animals on day 29 was found to be comparable similarly.

Hematological investigations:

The results of hematological investigations (Table 4) conducted on day 29 revealed following significant changes in the values of different parameters investigated when compared with those of respective controls; however, the increase or decrease in the values obtained was within normal biological and laboratory limits or the effect was not dose dependent.

Biochemical Investigations:

Results of Biochemical investigations conducted on days 29 and recorded in Table 2 revealed the following significant changes in the values of hepatic serum enzymes studied. When compared with those of respective control. However, the increase or decrease in the values obtained was within normal biological and laboratory limits.

Histopathology:

In histopathological examination, revealed normal architecture in comparison with control and treated animal.

DISCUSSION:

1) All the animals from control and all the treated dose groups up to 500 mg/kg survived throughout the dosing period of 28 days.

2) No signs of toxicity were observed in animals from different dose groups during the dosing period of 28 days.

3) Animals from all the treated dose groups exhibited comparable body weight gain with that of controls throughout the dosing period of 28 days.

4) Food consumption of control and treated animals was found to be comparable throughout the dosing period of 28 days

5) Haematological analysis conducted at the end of the dosing period on day 29, revealed no abnormalities attributable to the treatment.

6) Biochemical analysis conducted at the end of the dosing period on day 29 no abnormalities attributable to the treatment.

7) Organ weight data of animals sacrificed at the end of the dosing period was found to be comparable with that of respective controls.

8) Histopathological examination revealed normal architecture in comparison with control and treated animal.

SUMMARY AND CONCLUSION:

In conclusion **MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE** can be considered safe, as it did not cause either any lethality or adverse changes with general behavior of rats and also there were no observable detrimental effects (100 to 300 mg/kg body weight) over a period of 28 days. Our results have demonstrated that the **MATHIYOOSHNA RASAYANAM WITH HONEY/GHEE** is relatively safe when administered orally in rats.

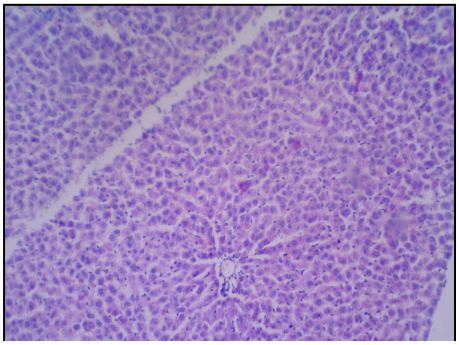
9.0 ABBRVIATION

No.	Number
Mg	Milligram
Kg	Kilogram
LD_{50}	Lethal Dose $_{50}$
p.o.	peros
mL	Milliliter

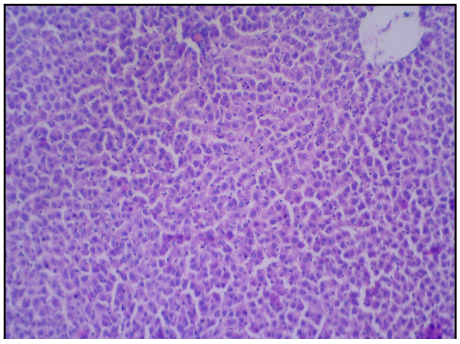
%	percentage
R&D	Research and Development
EDTA	Ethylene Diamine Tetra Acetic Acid
M	Male
g%	Gram percentage
g	Gram
NOAEL	No-Observed-Adverse-Effect-Level
MLD	Minimum Lethal Dose
MTD	Maximum Tolerated Dose
OECD	Organisation of Economic Co-operation and Development
CPCSEA	Committee for the Purpose of Control and Supervision of Experiments on Animals

HISTOPATHOLOGY - TOXICITY STUDY

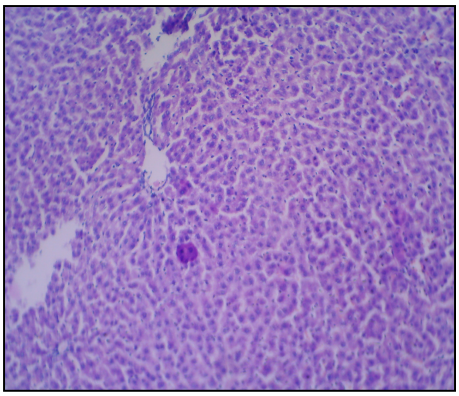
SPECIMEN : A) Liver. Group – : Mathiyooshna rasayanam



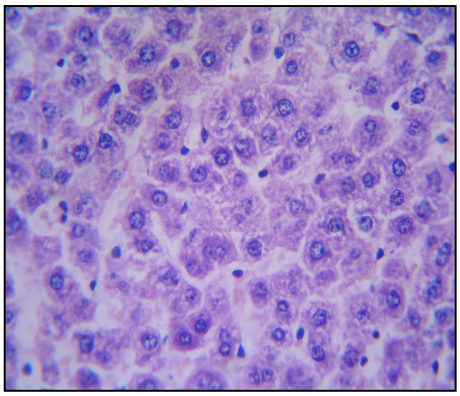
10x shows lobular architecture with central vein congestion



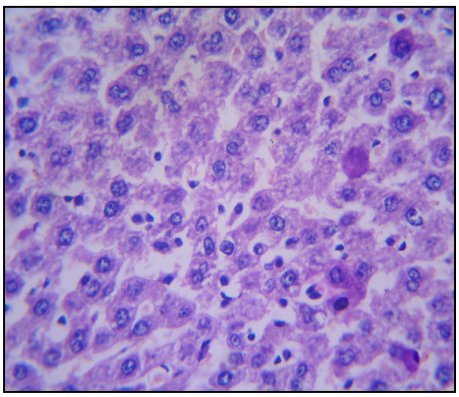
10x shows lobular architecture



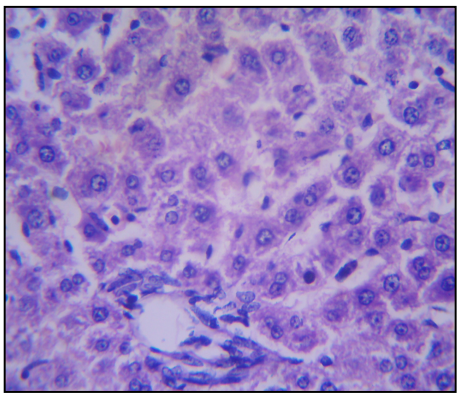
10x shows normal lobular architecture



40x normal hepatocytesshows



40x shows interface hepatitis



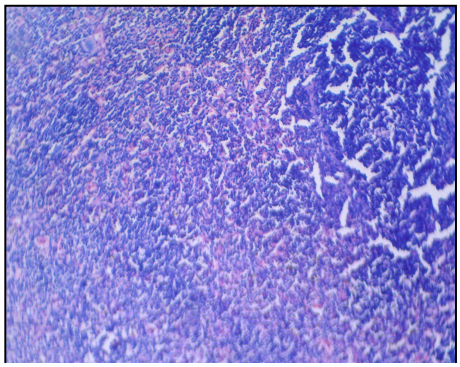
40x shows mild periportal inflammation (2)

MICROSCOPIC APPEARANCE:

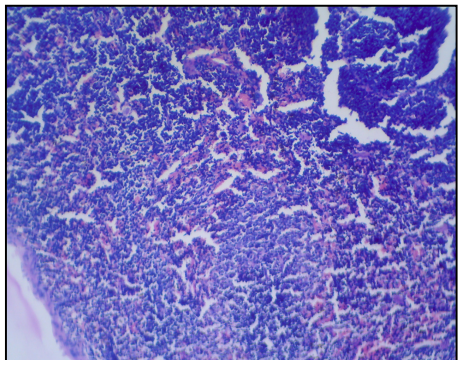
Section from liver shows lobular architecture with interface hepatitis. Individual Hepatocytes shows reactive atypia. Portal triad shows no significant pathology. Central vein and Sinusoids show dilatation.

SPECIMEN : B) spleen.

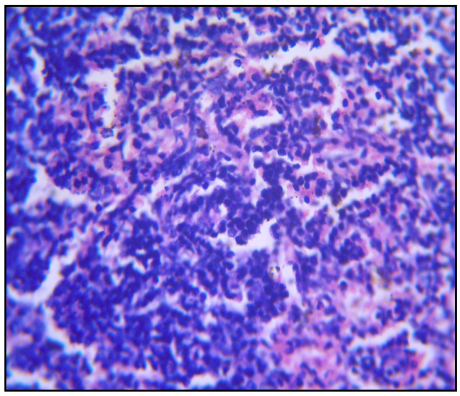
Group – : Mathiyooshna rasayanam



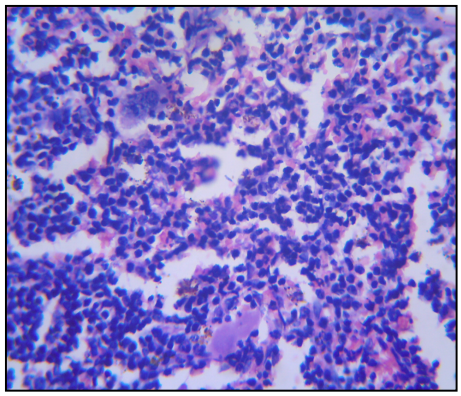
10x shows normal red and white pulp



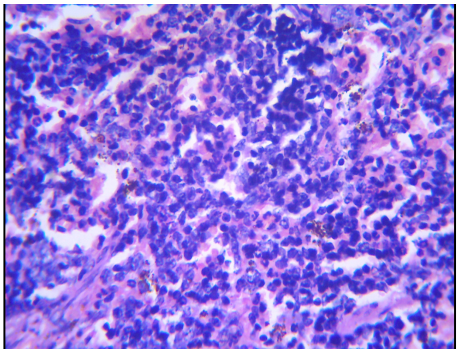
10x shows normal spleen



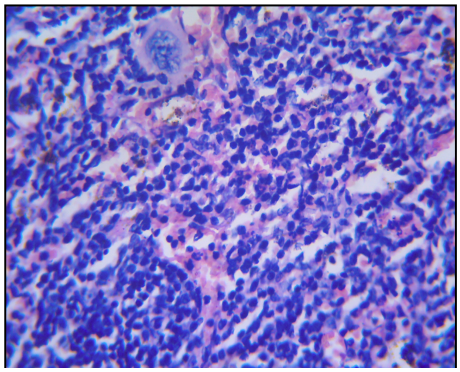
40 xshows normal lymphocytic infiltrates with megakaryocytes



40x shows megakaryocytes



40x shows normal morphology of white pulp



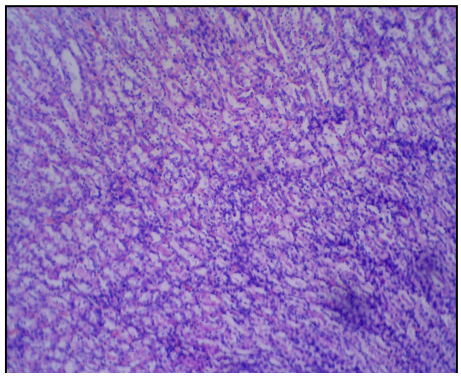
40x shows red pulp with lymphocytic infiltration

MICROSCOPIC APPEARANCE:

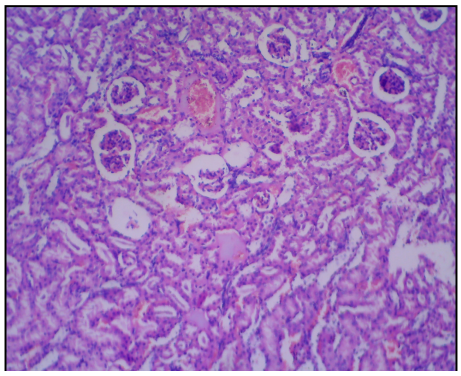
Section studied from spleen shows normal white pulp and red pulp. Red pulp shows pigment laden macrophages and congested vessels. White pulp shows lymphocytic infiltrates forming germinal centre. The pencillar artery shows normal morphology. Megakaryocytes

SPECIMEN : C) Kidney.

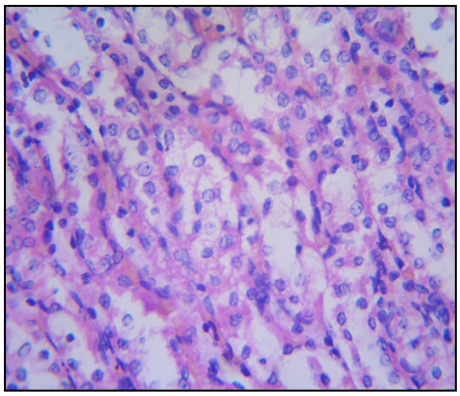
Group – : Mathiyooshna rasayanam



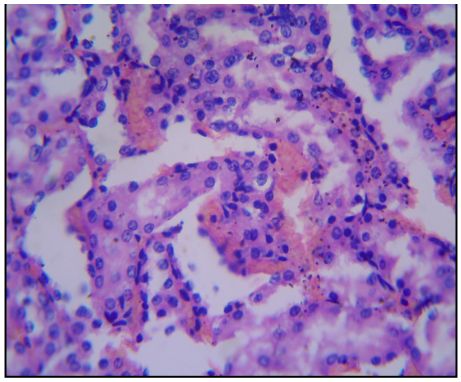
10x shows mild interstitial lymphocytic infiltration



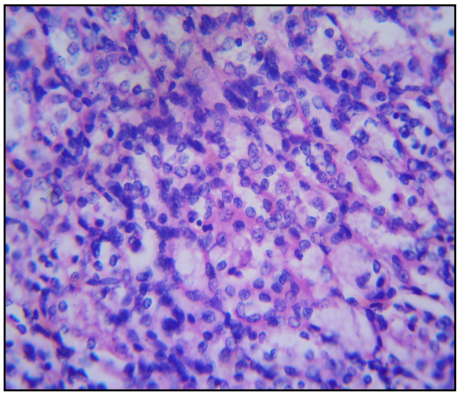
10x shows normal kidney cortex and medulla



40x hsows normal interstitium



40x shows blood vessels congestion



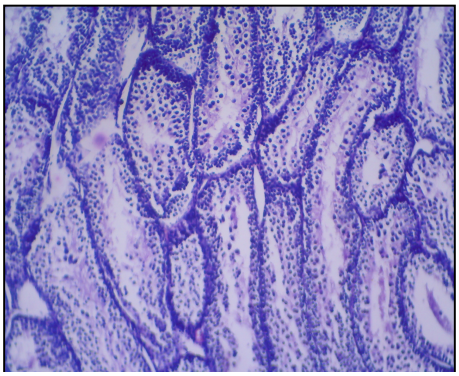
40x shows mild inflammation

MICROSCOPIC APPEARANCE:

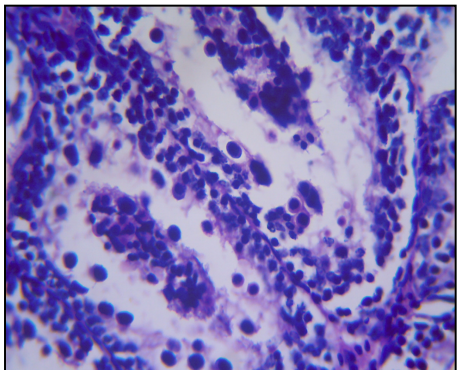
Section from kidney shows both cortex and medulla. Glomeruli and tubules shows no significant pathology. Interstitium shows no significant pathology. Blood vessels show congestion. There is no evidence of toxic changes.

SPECIMEN : D) Testis

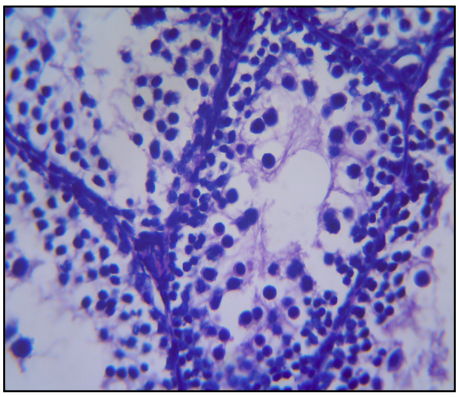
Group – : Mathiyooshna rasayanam



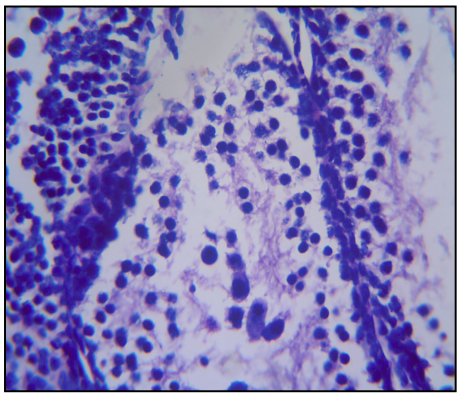
10x shows focal maturation arrest



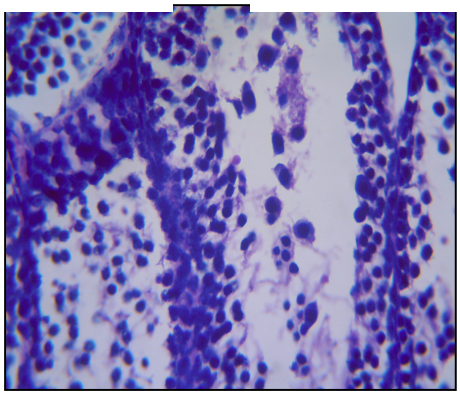
40x show smaturation arrest



40x shows normal semini ferous tubules



40x shows normal spermatogenesis



40x shows normal spermatogenesis

MICROSCOPIC APPEARANCE:

Section from testes with seminiferous tubules showing maturation arrest with lacking of spermatogenesis.

Name : **Ref. No. : [H0 332A/18]**	**Rec.On : 25/03/2018** **Rep.On : 18/04/2018**

HISTOPATHOLOGY

TOXICITY STUDY

SPECIMEN **:** Liver

Group – : Dr.Aysha- M.R.

GROSS APPEARANCE:

Received a specimen of liver measuring 3.5x2.3x1.2cms.

(PE): Two bits – One block.

MICROSCOPIC APPEARANCE:

Section from liver shows normal lobular architecture with mild interface hepatitis. Individual Hepatocytes shows no significant pathology. Portal triad shows mild periportal inflammation. Central vein shows dilated and congested. Sinusoids show dilatation.

Dr.C.R.Ajeethkumar.M.D. (Path).

Consultant pathologists:
Dr.S.Kalyani.M.D. (Path), Dr. C.R.Ajeeth kumar.M.D. (Path),

Checked

Name :	**Rec.On : 25/03/2018**
Ref. No. : [H0 332B/17]	**Rep.On : 18/04/2018**

HISTOPATHOLOGY

Toxicity study

SPECIMEN : B) Spleen.

Group – : Dr.Aysha- M.R.

GROSS APPEARANCE:

Received a specimen of spleen measuring 2.6x0.9x0.4cms.

(PE): Two bits – One block.

MICROSCOPIC APPEARANCE:

Section studied from spleen shows normal white pulp and red pulp. Red pulp shows pigment laden macrophages and congested vessels. White pulp shows lymphocytic infiltrates forming germinal centre. The pencillar artery shows normal morphology. Megakaryocytes are also seen. There is no evidence of toxic changes.

Dr.C.R.Ajeeth kumar. M.D. (Path),

Consultant pathologists:
Dr.S.Kalyani.M.D. (Path), Dr. C.R.Ajeeth kumar.M.D. (Path),

Checked

Name :	**Rec.On : 25/03/2018**
Ref. No. : [Ho 332C/18]	**Rep.On : 18/04/2018**

HISTOPATHOLOGY

Toxicity study

SPECIMEN : Kidney.

Group – : Dr.Aysha- M.R.

GROSS APPEARANCE :

Received specimen of kidneys each measuring 1.2x0.6x0.5cms and 1.2x0.5x0.5cms.

PE : Two bits – One block.

MICROSCOPIC APPEARANCE:

Section from kidney shows both cortex and medulla. Glomeruli and tubules show no significant pathology. Interstitium shows mild lymphocytic infiltrates. Blood vessels show congestion. There is no evidence of toxic changes.

Dr. C.R.Ajeeth kumar.M.D. (Path).

Consultant pathologists:
Dr.S.Kalyani.M.D. (Path), Dr. C.R.Ajeeth kumar.M.D. (Path),

Checked

Name :	**Rec.On : 25/03/2018**
Ref. No. : [Ho 332D/18]	**Rep.On : 18/04/2018**

HISTOPATHOLOGY

Toxicity study

SPECIMEN : Testis.

Group – : Dr.Aysha- M.R.

GROSS APPEARANCE :

Received specimen of both testis measuring each 1.0x0.7x0.5cms and 1.0x0.6x0.5cms.

PE : Two bits – One block.

MICROSCOPIC APPEARANCE:

Section from testes with focal seminiferous tubules shows maturation arrest with lacking of spermatogenesis. No evidence of granuloma/ malignancy

Dr. C.R.Ajeeth kumar.M.D. (Path).

Consultant pathologists:
Dr.S.Kalyani.M.D. (Path), Dr. C.R.Ajeeth kumar.M.D. (Path),

ANNEXURE –V
ASSESSMENT FORMS

FORM I **:** Screening and Selection Proforma

FORM I A **:** History Proforma on Enrollment

FORM II : Clinical assessment on enrollment

FORM II A **:** Clinical assessment during and after trial

FORM III : Laboratory Investigation on enrollment and conclusion of trial

FORM IV : Consent Form

FORM IV B : Withdrawal form

FORM IV C : Patient information sheet

FORM IV D : Dietary Advice form

FORM IV E : Adverse Reaction form

FORM IV F : Discharge proforma

GOVERNMENT SIDDHA MEDICAL COLLEGE & HOSPITAL

POST GRADUATE DEPARTMENT

PALAYAMKOTTAI, TIRUNELVELI – 627002

BRANCH – III SIRAPPU MARUTHUVAM

A PHASE II CLINICAL STUDY TO EVALUATE THE THERAPEUTIC EFFICACY OF SIDDHA FORMULATION "**MATHIYOOSHNA RASAYANAM**" INTERNAL & "**NYMPATHY THYLAM**" EXTERNAL IN "**UTHIRA VATHA SURONITHAM**" (RHEUMATOID ARTHRITIS).

FORM I – SCREENING & SELECTION PROFORMA

1. OP / IP NO : _____
2. NAME : _____
3. RELIGION : H / C / M / O
4. AGE / GENDER : _____
5. OCCUPATION : _____
6. INCOME : _____
7. CONTACT NO : _____
8. INCLUSION CRITERIA :

INCLUSION CRITERIA :

- Age : 18-60 years
- Sex : Both Male and Female
- Symmetrical joint involvement
- Arthritis of 3 or more joints
- Rheumatoid factor positive or negative
- Morning stiffness
- Swelling especially in the inter Phalangeal joint.
- Patients who are willing for admission and stay in ipd for 48 days or willing to attend OPD
- Patient who are willing to undergo radiological investigation and give blood and urine samples for laboratory investigation.

- Patient willing to sign the informed consent stating than he/she will consciously stick to the treatment during 48 days but can opt out of the trial of his/her own conscious discretion.

EXCLUSION CRITERIA :

- Hypertension and other cardial ailments.
- Diabetes mellitus
- Narcotics
- Alcoholics and smokers
- Pregnancy and lactation
- History of trauma
- Neurological disorder
- Tuberculosis
- Any other serious illness
- Psoriatic arthritis
- Gouty arthritis

ADMITTED TO TRIAL:

YES NO

If Yes Serial Number :

Date :

Station:

Signature of the Investigator :

Signature of the Lecturer : **Signature of the HOD**

GOVERNMENT SIDDHA MEDICAL COLLEGE & HOSPITAL

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BRANCH – III SIRAPPU MARUTHUVAM

A PILOT STUDY TO EVALUATE THE THERAPEUTIC EFFICACY OF SIDDHA FORMULATION "**MATHIYOOSHNA RASAYANAM**" INTERNAL & "**NYMPATHY THYLAM**" EXTERNAL IN "**UTHIRA VATHA SURONITHAM**" (RHEUMATOID ARTHRITIS).

FORM I A – HISTORY PROFORMA

1. SL.NO : _____
2. OP / IP NO : _____
3. NAME : _____
4. RELIGION : H / C / M / O
5. AGE / GENDER : _____
6. OCCUPATION : _____
7. INCOME : _____
8. CONTACT NUMBER : _____
9. MARITAL STATUS : Married / Unmarried
10. COMPLAINTS & DURATION :

11. PERSONAL HISTORY:

PERSONAL HABITS	YES	NO	IF YES SPECIFY DURATION
Smoking			
Tobacco Chewing			
Alcohol			
Narcotic Drug Addiction			

12. DRUG HISTORY:

Whether the Patient has underwent any allopathic Treatment

1. Yes 2. No.

If yes specify the nature of the drug and treatment duration _____

13. FAMILY HISTORY:

Whether this problem runs in family?

1. Yes 2. No

If yes, mention the relationship of affected person(s)

1. _____
2. _____

14. DIETARY HABITS :

1. Pure vegetarian ☐
2. Non-Vegetarian ☐

Date :

Station:

Signature of the Investigator :

Signature of the Lecturer : **Signature of the HOD**

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BRANCH – III SIRAPPU MARUTHUVAM

A PILOT STUDY TO EVALUATE THE THERAPEUTIC EFFICACY OF SIDDHA FORMULATION "**MATHIYOOSHNA RASAYANAM**" INTERNAL & "**NYMPATHY THYLAM**" EXTERNAL IN "**UTHIRA VATHA SURONITHAM**" (RHEUMATOID ARTHRITIS).

FORM II AND II-A CLINICAL ASSESSMENT ON ENROLLMENT AND ON VISITS

1.	OP / IP No	:
2.	BED No	:
3.	SL. NO	:
4.	NAME	:
5.	AGE	:
6.	GENDER	:
7.	OCCUPATION	:
8.	SOCIAL STATUS	:
9.	DATE OF ADMISSION	:
10.	DATE OF DISCHARGE	:
11.	POSTAL ADDRESS	:
12.	COMPLAINTS & DURATION	:
13.	HISTORY OF PRESENT ILLNESS	:
14.	PAST HISTORY	:
15.	FAMILY HISTORY	:

16. MENSTRUAL HISTORY (If Applicable):

17. HABITS:

1. Smoker :
2. Alcoholic :
3. Tobbaco chewer :
4. Betel nut chewer :
5. Non-Vegetarian :
6. Drug addiction :

18. GENERAL EXAMINATION:

1. Body weight (Kg) :
2. Height (Cm) :
3. Body Temperature (F) :
4. Blood Pressure (mmHg) :
5. Pulse Rate (/min) :
6. Heart Rate (/min) :
7. Respiratory Rate (/min) :
8. Pallor :
9. Jaundice :
10. Clubbing :
11. Cyanosis :
12. Pedal Oedema :
13. Lymphadenopathy :
14. Jugular venous pulsation :

19. CLINICAL EXAMINATION:

I. INSPECTION:

1. Attitude :
2. Muscular spasm :
3. Muscle wasting – Proximal :
4. Muscle wasting – Distal :
5. Minor Joint Swelling :
6. Major Joint Swelling :
7. Nodules :
8. Deformity :

II. PALPATION:

1. Swelling :
2. Tenderness :
3. Joint Stiffness :
4. Muscle wasting :
5. Local heat :
6. Local Lymphadenopathy :
7. Pitting Oedema :
8. Nodules :

III. MOVEMENTS:

Restriction of joint movements

1.	Neck	:	Full	Partial
2.	Shoulder	:		
3.	Elbow joint	:		
4.	Knee joint	:		
5.	Ankle joint	:		
6.	Hip joint	:		
7.	Minor joints	:		

IV. PAIN:

1.	Onset :	Sudden	:	Gradual	:	
2.	Early morning stiffness :	Present	:	absent	:	
3.	Nature of pain:	Mild	:	Moderate	:	Severe:
4.	Aggravating factor –Movements		:			
5.	Relieving factor – rest		:			
6.	Stiffness		:			
7.	Tenderness		:			

V. CLINICAL ASSESSMENT :

1. Arthritis of three or more Joints :
2. Arthritis of hand joints :
3. Morning Stiffness :
4. Fever :
5. Anorexia :
6. Anaemia :
7. Spindle appearance of fingers :
8. Restricted movements :
9. Rheumatoid Nodules :
10. Numbness :

20. EXAMINATION OF OTHER SYSTEMS:

1. CVS :
2. RS :
3. CNS :
4. ABDOMEN :
5. GENITO – URINARY :

EXAMINATION – SIDDHA ASPECTS

1. NILAM:

1. Kurinji 2. Mullai 3. Marutham 4. Neithal 5. Paalai

2. KAALAM:

1. Kaar Kaalam 2. Koothir Kaalam 3. Munpani Kaalam
4. Pinpani Kaalam 5. Elavenir Kaalam 6. Mudhuvenir Kaalam

3. YAAKKAI:

1. Vatham	2. Pitham	3. Kabam
4. Vathapitham	5. Pithavatham	6. Kabavatham
7. Vathakabam	8. Pithakabam	9. Kabapitham

4. GUNAM:

1. Sathuvam	2. Rasatham	3. Thamasam

5. KANMENDHIRIUM / KANMAVIDAYAM

1. Kai :
2. Kaal :
3. Vaai :
4. Eruvaai :
5. Karuvaai :

6. UYIR THATHUKKAL:

I. VATHAM:

1. Piraanan :
2. Abaanan :
3. Viyaanan :
4. Uthaanan :
5. Samaanan :
6. Naagan :
7. Koorman :
8. Kirukaran :
9. Devathathan :
10. Dhananjeyan :

II. PITHAM :

1. Analagam :
2. Ranjagam :
3. Saathagam :
4. Aalosagam :
5. Praasagam :

III. KABAM:

1. Avalambagam :
2. Kilethagam :
3. Pothagam :
4. Tharpagam :
5. Santhigam :

7. UDAL THAATHUKKAL:

1. Saaram :
2. Senneer :
3. Oon :
4. Kozhuppu :
5. Enbu :
6. Moolai :
7. Sukkilam / Suronitham:

8. ENVAGAI THERVUGAL:

1. Naadi :
2. Sparisam :
3. Naa :
4. Niram :
5. Mozhi :
6. Vizhi :
7. Malam :

   i. Niram: ii. Thanmai: iii. Irugal: iv.Ilagal:

8. Moothiram :

I. NEERKURI:

a. Niram :

b. Manam :

c. Edai :

d. Nurai :

e. Enjal :

II. NEIKURI:

Vatha Neer : Pittha Neer : Kaba Neer :

Date :

Station:

Signature of the Investigator :

Signature of the Lecturer : **Signature of the HOD**

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BRANCH – III SIRAPPU MARUTHUVAM

A PHASE II CLINICAL TRIAL TO EVALUATE THE THERAPEUTIC EFFICACY OF SIDDHA FORMULATION "**MATHIYOOSHNA RASAYANAM**" INTERNAL & "**NYMPATHY THYLAM**" EXTERNAL IN "**UTHIRA VATHA SURONITHAM**" (RHEUMATOID ARTHRITIS).

FORM III – LABORATORY INVESTIGATION

1. BLOOD:
   1. TC : (Cells / Cumm)
   2. DC (%) : N : L : M : E :
   3. ESR (mm) : ½ hr : 1 hr :
   4. Hb :
   5. Blood Sugar : a) Fasting : b) Post Prandial :
   6. Renal function tests:
      Blood Urea: Serum creatinine:
   7. Lipid profile :
      HDL: LDL: VLDL:
      Total Cholesterol : TGL :
   8. Liver Function tests:
      Serum Bilirubin : Total Direct Indirect

SPECIFIC INVESTIGATIONS

RA factor :

ASO titre :

C-Reactive Protein :

SGOT :

SGPT :

Serum albumin & globulin :

Total protein :

II. URINE:

1. Albumin :
2. Sugar :
3. Epithelial cells :
4. Pus cells :
5. Red blood cells :
6. Casts / Crystals :

III. MOTION:

1. Ova :
2. Cyst :
3. Occult blood :
4. Pus cells :

IV. X-RAY FINDINGS

Date :

Station:

Signature of the Investigator :

Signature of the Lecturer : **Signature of the HOD**

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FORM IV A – CONSENT FORM

CERTIFICATE BY INVESTIGATOR

I certify that I have disclosed all the details about the study in the terms readily understood by the patient.

Signature _____

Date _____

Name _____

CONSENT BY PATIENT

I have been informed to my satisfaction, by the attending physician, the purpose of the clinical trial, and the nature of drug treatment and follow-up including the laboratory investigations to be performed to monitor and safeguard my body functions.

I am aware of my right to opt out of the trial at any time during the course of the trial without having to give the reasons for doing so.

I exercising my free power of choice, hereby give my consent to be included as a subject in the clinical trial of "MATHIYOOSHNA RASAYANAM" (Internal drug) and "NYMPATHY THYLAM" (External drug) for the treatment of "UTHIRA VATHA SURONITHAM" (RHEUMATOID ARTHRITIS)".

Place :

Date :

Signature :

Name :

Witness Signature:

Name :

அரசினர் சித்த மருத்துவக் கல்லூரி மற்றும் மருத்துவமனை
பாளையங்கோட்டை
பட்டமேற்படிப்பு சிறப்பு மருத்துவத்துறை

"மதியூஷ் ண ரசாயனம்" மற்றும் "நிம்பாதி தைலம்" இவற்றின் பரிகரிப்புத் திறனைக் கண்டறியும் மருத்துவ ஆய்வு ஒப்புதல் படிவம் ஆய்வாளரால் சான்றளிக்கப்பட்டது.

நான் இந்த ஆய்வைக் குறித்த அனைத்து விபரங்களையும் நோயாளிக்கு புரியும் வகையில் எடுத்துரைத்தேன் என உறுதியளிக்கிறேன்.

தேதி : கையொப்பம்:

இடம் : பெயர்:

நோயாளியின் ஒப்புதல்

என்னிடம் இந்த மருத்துவ ஆய்வின் காரணத்தையும் மருந்தின் தன்மை மற்றும் மருத்துவ வழிமுறையைப் பற்றியும் தொடர்ந்து எனது உடல் இயக்கத்தை கண்காணிக்கவும், அதனைப் பாதுகாக்கவும் பயன்படும் மருத்துவ ஆய்வுக்கூட பரிசோதனைகள் பற்றியும் திருப்தி அளிக்கும் வகையில் ஆய்வு மருத்துவரால் விளக்கிக் கூறப்பட்டது.

நான் இந்த மருத்துவ ஆய்வின் போது காரணம் எதுவும் கூறாமல் எப்பொழுது வேண்டுமானாலும் இந்த ஆய்விலிருந்து என்னை விடுவித்துக் கொள்ளும் உரிமையை தெரிந்திருக்கின்றேன்.

நான் என்னுடைய சுதந்திரமாகத் தேர்வு செய்யும் உரிமையைக் கொண்டு **உதிர வாத சுரோணிதம்** என்னும் நோய்க்கான **மதியூஷ்ண ரசாயனம்** மற்றும் **நிம்பாதி தைலம்** ஆகியவற்றின் பரிகரிப்புத் திறனைக் கண்டறியும் மருத்துவ ஆய்விற்கு என்னை உட்படுத்த ஒப்புதல் அளிக்கிறேன்.

தேதி : கையொப்பம்:

இடம் : பெயர் :

சாட்சிக்காரர் கையொப்பம்:

பெயர் :

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BRANCH – III SIRAPPU MARUTHUVAM

A PHASE II CLINICAL TRIAL TO EVALUATE THE THERAPEUTIC EFFICACY OF SIDDHA FORMULATION "**MATHIYOOSHNA RASAYANAM**" INTERNAL & "**NYMPATHY THYLAM**" EXTERNAL IN "**UTHIRA VATHA SURONITHAM**" (RHEUMATOID ARTHRITIS).

FORM IV B – WITHDRAWAL FORM

1. SL.NO : _____
2. OP / IP NO : _____
3. NAME : _____
4. RELIGION : H / C / M / O
5. AGE / GENDER : _____
6. OCCUPATION : _____
7. SOCIAL STATUS : _____
8. CONTACT NO : _____
9. DATE OF TRIAL COMMENCEMENT : _____
10. DATE OF WITHDRAWAL FROM TRIAL : _____
11. REASONS FOR WITHDRAWAL : _____
    - Long absence at reporting : Yes / No
    - Irregular treatment : Yes / No
    - Shift of locality : Yes / No
    - Increase in severity of symptoms : Yes / No
    - Development of severe adverse drug reactions: Yes / No

Date :

Station:

Signature of the Investigator :

Signature of the Lecturer : **Signature of the HOD**

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FORM IV C – DRUG COMPILANCE FORM

Name of the Drug : JATHIPALATHI CHOORANAM

Drugs issued : (Mg / Gram)

Drugs returned : (Mg / Gram)

S. NO	**DATE**	**DRUG TAKEN TIME**	
		MORNING / TIME	**EVENING / TIME**
Day 1			
Day 2			
Day 3			
Day 4			
Day 5			
Day 6			
Day 7			
Day 13			
Day 14			
Day 15			
Day 16			
Day 17			
Day 18			
Day 19			

Day 25			
Day 26			
Day 27			
Day 28			
Day 29			
Day 30			
Day 31			
Day 37			
Day 38			
Day 39			
Day 40			
Day 41			
Day 42			
Day 43			
Day 44			
Day 45			
Day 46			
Day 47			
Day 48			

Date :

Station:

Signature of the Investigator :

Signature of the Lecturer : **Signature of the HOD**

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- PARARASA SEKARAM
- AGATHIAR-2000
- SATHAGANAADI
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INGREDIENTS OF MATHIYOOSHNA RASAYANAM

Valuzhuvai

Sathipathiri

Thippili

Omam

Lavangapattai

Parangipattai

Thippilimoolam

Annachipoo

Nellivattral

Elam

Vaividangam

Kadukkai

Kaatu Milagu

Nannari

Arathai

Seeragam

Milagu

Kurosani omam

Vetpalai arisi

Kostam

Athimathuram

Chukku

Cheviyam

Kanduparangi

Santhanam

Koraikilangu

Sadamanjil

Kirambu

Thandrikai

INGREDIENTS OF MATHIYOOSHNA RASAYANAM

Erukku

Sathurakalli

Maa

Yetti

Nallennai

Veppaennai

MATHIYOOSHNA RASAYANAM (Internal)

NYMPATHY THYLAM (External)

INTERNATIONAL JOURNAL OF ADVANCED MULTIDISCIPLINARY RESEARCH (IJAMR)
ISSN:2393-8870
www.ijarm.com
IMPACT FACTOR: 3.565, ICV:80.43(2016)

DARSHAN PUBLISHERS

Editorial Board Member of
International Journal of Advanced Multidisciplinary Research (IJAMR)
is hereby awarding this certificate to

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In recognition of the publication of the paper entitled **"Review on single plant for the management of Amenorrhoea"** published in IJAMR Journal, Volume: 5, Issue: 4, Year: 2018.

Managing Editor
DARSHAN PUBLISHERS
8/173, Vengayapalayam,
Seerappalli (Po.), Rasipuram (Tk.),
Namakkal (Dt.)-637 406.
Tamil Nadu, India.

Editor in Chief
IJAMR
Website : www.ijarm.com
E-mail: editorijarm@gmail.com

INTERNATIONAL JOURNAL OF CURRENT RESEARCH IN MEDICAL SCIENCES
ISSN:2454-5716
P-ISJN: A4372-3064, E -ISJN: A4372-3061
www.ijcrims.com
Impact Factor: 4.363, ICV :80.68 (2016)

PUBLICATION CERTIFICATE

Editorial Board Member of

International Journal of Current Research in Medical Sciences

is hereby awarding this certificate to

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In recognition of the publication of the paper entitled **"Antioxidant activity of Mathiyooshna Rasayanam"** published in IJCRMS Journal, Volume: 4, Issue: 5, Year: 2018.

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